The Use of Neuromuscular Blockers and Advanced Sedation by Field EMT-Paramedics to Promote More Effective Airway Management in Adult Trauma Patients With Glasgow Coma Scale of 8 or Less

Succinylcholine
Rocuronium
Midazolam

EMT-P Trial Study Proposal
County of San Diego Department of Health Services
Division of Emergency Medical Services

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Overview

The San Diego County Division of Emergency Medical Services proposes to undertake a prospective, matched cohort study of the effectiveness of two neuromuscular blocking (NMB) agents and a single amnesic/sedative in promoting increased effectiveness of field airway management among certain adult trauma patients. These pharmaceuticals would be used in implementing advanced airway techniques, such as rapid sequence intubation (RSI) and hyperventilation by EMT-Paramedics (EMT-Ps) in the field. This proposal involves an 18 month study period, with an anticipated 18 month continuation.

Specifically, the Division of EMS proposes to study the following hypothesis:

> "The use of neuromuscular blockers and advanced sedation by EMT-Paramedics can improve airway management in the field and decrease hypoxia-mediated brain injury in adult (age ≥ 18 years) Trauma Center Candidates with a Glasgow Coma Scale ≤8."

The medications to be evaluated are:

1. Succinylcholine
2. Rocuronium (Zemuron™)
3. Midazolam (Versed™)

In San Diego County, prehospital RSI (which requires neuromuscular blockade) has been available to patients only through the involvement of the County's advanced life support air medical provider(s). These providers, which have used registered nurses or flight physicians to provide this treatment intervention, serve as flight crews for on-scene air medical support. Because neuromuscular blockers are not included in the California Scope of Practice for EMT-Paramedics (nor have they been formally evaluated for possible inclusion into the California EMT-P Scope of Practice), they have not been available to patients receiving care and transport in paramedic ground ambulances.

An airway management study, undertaken by the County's Prehospital Audit Committee (which advises the EMS Medical Director on issues relating to prehospital care) and the Base Station Physicians Committee, has identified that the care of adult trauma center candidates with a Glasgow Coma Score of 8 or less might be improved through more aggressive advanced airway management. Up to 50% of this patient population does not arrive at the receiving hospital's emergency department with an endotracheal tube. Generally, the primary reasons for non-intubation of these patients (no attempt or unsuccessful attempt) were (1) the patient's gag reflex, (2) clenched teeth, (3) management difficulties, and (4) short ETA to receiving trauma

center. It is thought that the addition the drugs and skills proposed will allow paramedics to quickly obtain control of the patients' airways and thereby improve oxygenation and outcomes.(See Fig.1.)

Figure 1 **San Diego County**
Intubation success on trauma patients, based on Glasgow Coma Score (GCS). 1/1/95 through 6/30/95

Glasgow Coma Score	Number of cases	Intubations Successful	Unsuccessful	No attempt	% Successful
8	11	1	1	9	9%
7	17	3	5	9	18%
6	8	3	0	5	38%
5	4	2	1	1	50%
4	6	1	4	1	17%
3	71	44	14	13	50%

(Note: In GCS=3, the patients who were dead on scene were excluded in the above numbers. These included 10 successful intubations, 2 unsuccessful intubations, 13 not attempted.)

This population is almost universally intubated immediately upon delivery to a trauma center, yet current San Diego County data demonstrate only 50% arrive at a trauma center with an endotracheal tube. Medical literature supports intubation of these patients such that the damaging effects of hypercarbia and hypoxia may be minimized. Indeed, hyperventilation is still a field intervention expected of head injured patients with altered level of consciousness (LOC).

1. A description of the procedure(s) or medication(s) proposed, the medical conditions for which they can be utilized, and the study population that will benefit.

The County of San Diego proposes to implement an 18 month (with an anticipated 18 month continuation), prospective, matched cohort trial study to evaluate the effectiveness of three medications (currently not within the Scope of Practice for EMT-Paramedics) in improving the airway management efforts in certain patients in the field. These medications are:

1. Succinylcholine
2. Rocuronium
3. Midazolam

These medications will be used to facilitate the insertion of an endotracheal tube for airway management prior to delivery of the patient to the receiving trauma center.

The population to be included in this study will include adult (18 years or greater) trauma patients who present to the 9-1-1 system with a Glasgow Coma Scale of 8 or less.

2. A compendium of studies and material from the medical literature

The classes of medications proposed in the study are not new to emergency medicine and are well described in the literature. Benzodiazepines (midazolam) and neuromuscular blockers (succinylcholine, rocuronium) are well known among emergency department physicians and anesthesiologists. Their value in assisting emergency physicians, anesthesiologists, and air medical providers in gaining and maintaining of critical patients' respiratory status is unquestioned.

Rationale for immediate control of patient's respiratory status (trauma patients with GCS 8 or less)

"Head injury is the leading cause of all trauma-related deaths."[1]

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[1]McGinnis, Trauma Nursing, WB Saunders Company, 1988, p365.

"Hypoxia and hypotension [are] independently associated with significant increases in morbidity and mortality from severe head injury.[2]"

"A controlled rapid sequence intubation is the best method of simultaneously establishing an airway and protecting the patient from potentially harmful effects of increased ICP.[3]"

Almost half (46%) of this population will experience some sort of hypoxia during the early post-traumatic period.[4]

Discussion - rationale for testing the three medications to be evaluated

Succinylcholine (Anectine™) is an ultra short-acting depolarizing-type, skeletal muscle relaxant for intravenous administration. Its onset of flaccid paralysis is rapid (within 1 minute of intravenous administration), and with single administration lasts approximately 4-6 minutes[5]. The ultra short period of activity makes this the neuromuscular blocker of choice in the field. Its short duration of action allows the field paramedic to quickly gain control of the patient's airway, but allows for rapid recovery of the patient from neuromuscular blockade in case airway interventions are unsuccessful.

Rocuronium (Zemuron™) is a non-depolarizing neuromuscular blocking agent with a rapid to intermediate onset (1-2 minutes to maximum block after intravenous administration) and a duration of action of approximately 33 minutes.[6] The proposed study protocols allow rocuronium to be used on patients who have been successfully intubated to facilitate transport without frequent re-bolusing of succinylcholine. This should minimize the increase in ICP

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[2]Chesnut, Marshall, et al, "The Role of Secondary Brain Injury in Determining Outcome from Severe Head Injury", Journal of Trauma, Vol. 32, No. 2, p. 216.

[3]Olshaker, JS, *et al*: Head Trauma Emergency Medicine Clinics of North America - Advances in Trauma, Vol. 11, Number 1, Feb 93, p 169.

[4]Chesnut, Marshall, et al. p 220.

[5] Product Insert, Succinylcholine Chloride, Organon Inc, June 1991.

[6]Product Information Insert, Zemuron, Organon, Inc., December, 1994.

associated with the neuromuscular blocker wearing off prior to delivery to a trauma center.

Midazolam (Versed™) is a short-acting benzodiazepine central nervous system depressant. Sedation after IV injection is achieved within 3 - 5 minutes. Full recovery from IV midazolam sedation generally is seen 2 hours after IV administration.[7] Midazolam is commonly used in the hospital setting because of its minimal impact on respiratory drive. The administration of an amnesic/sedative prior to NMB is a common practice in the emergency department, and is provided as a humanitarian effort to limit the patients' experience of NMB.

Additional references from the medical literature are presented in the attachments to this document.

3. A description of the proposed study design including the scope and method of evaluation the effectiveness of the procedure(s) or medication(s) and the expected outcome.

As proposed for the San Diego County trial study, succinylcholine, rocuronium and midazolam will be incorporated into the treatment protocols for certain adult trauma center candidates such that rapid sequence intubation may become available to the field paramedic. Paramedics will document their justification to implement these medications and skills as opposed to intubation without NMB. These justifications include:

1. initial attempts at intubation without neuromuscular blockers fail, or
2. the patient is exhibiting signs that indicate endotracheal intubation without NMB would be difficult (agitation, uncooperative, etc.), or
3. the patient is clenching teeth such that no ET attempt can be made without NMB, or
4. the intubated patient becomes unmanageable for transport.

By definition, the medications will be used only upon patients in severe crisis when any delay in airway management might pose a threat to the patient, therefore, these medications will be

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[7]1992 Physicians' Desk Reference, Roche Labs, Versed, p 1924.

used by participating paramedics upon "standing order" to optimize airway control and scene time.

Provider agency eligibility to participate in study

The personnel to be included in this study will include personnel from any ALS provider agency that meets the following criteria:

1. Pulse oximetry capability.
2. Ability to enter study data directly into the County's computerized Quality Assurance Network.
3. Commitment to comply with medication storage requirements and procedures.
4. Commitment to support personnel training activities.
5. Commitment to cooperate in the investigation of incidents with EMS agency and base hospital personnel.
6. Commitment to provide ancillary equipment (such as in-line colormetric end-tidal CO2 detectors).

Field Personnel to participate in study

Any licensed and locally accredited EMT-Paramedic who successfully completes the prescribed training program, agrees to comply with study requirements, and is working for a participating ALS provider agency may participate in the study.

Data Collection

The San Diego County Quality Assurance Network (QA-Net) provides real time, on-line communication among virtually all base hospitals, receiving hospitals, dispatch centers, many ALS provider agencies, and the EMS office. Among the capabilities of the QA-Net is the capacity for EMT-Paramedics and Mobile Intensive Care Nurses (MICNs) to generate a computerized patient record, immediately following service, in a paperless environment. The QA-Net can be configured to accept additional data from the paramedic directly on its "research screens." Additionally, the paramedic will be required to complete a NMB/RSI Study worksheet (see attachments) to record additional data points, and additional data will be collected from the San Diego County Trauma Registry.

Patients enrolled in the study will be matched with cases found in the San Diego Trauma Registry to serve as the control group.

Evaluation

Evaluation of data collected will be coordinated by the San Diego Division of Emergency Medical Services, and will include the following components:

Concurrent:

1. Immediate notification and review of each individual case by the EMS Medical Director as each study participant is enrolled by field personnel.

2. Ongoing collection and trending of field data by EMS bio-statistical and clinical personnel.

Retrospective:
The evaluation of the study will focus on the following questions.

Study Question	Evaluation Data Points
1. Compared to baseline data on the intubation rate for adult patients with a GCS≤8 within the San Diego County EMS system, does the use of neuromuscular blockers increase the rate that these patients arrive to the ED successfully intubated?	Successful ET field intubation Number of intubation attempts Number of attempts prior to NMB Use of NMB after ET insertion? Arrive ED with tube?
2. For all patients enrolled in the study, does pulse oximetry demonstrate an improved oxygen saturation upon delivery to the ED in those patients intubated, versus those not intubated, using NMB?	O2 Saturation as measured before initial NMB O2 saturation measured within 5 minutes of initial NMB O2 saturation measured in ambulance upon arrival to ED
3. Are scene times prolonged when neuromuscular blockers are initiated in the field? Is this significant to patient care??	Arrive Scene time / Depart scene time NMB attempted Successful intubation achieved in field Tube still in place at ED
4. Is there increased morbidity or mortality associated with the use of neuromuscular blockade in the field?	ED Outcome Trauma Registry Complication List Discharge outcome

5.	Is there an improved discharge functional capacity among patients treated in the field with NMB (versus those in the matched case controls).	Trauma Registry

If, during the study period, increased morbidity or mortality is demonstrated (as compared to baseline data), the study will be immediately suspended and continuation of the study will be re-evaluated by the EMS Medical Director. It is recognized that this group of patients is, by nature, extremely unstable, and that some of the patients enrolled in the study will have poor outcomes regardless of the field use of NMB. We will attempt to evaluate the exact cause of any morbidity or mortality seen to determine if study protocols and training efforts remain appropriate.

4. Recommended policies and procedures to be instituted by the local EMS agency regarding the use of medical control of the procedure(s) or medication(s) used in the study.

The medical control issues regarding the study are outlined completely in Attachment I of this document. This attachment includes:

Study Protocol Summary
Master Study Research Protocol (for submission to Trauma Center Investigative Review Boards)
Standing Orders for Field Treatment
EMT-Paramedic data collection worksheet

5. A description of the training and competency testing required to implement the study

The proper training and testing of field paramedics in the medications and skills proposed is recognized as the key to the implementation of a successful study. Therefore, significant

efforts have been made to ensure the highest quality of prehospital education for the field personnel participating.

The training curriculum will focus on the following topics:

1. Assessment - EMT-Paramedics, as an essential component of their job, are continually asked and expected to assess patients with compromise to their respiratory system. This training includes the ability to assess the effectiveness of spontaneous respirations, the need for external respiratory support, the effectiveness of respiratory support, circulatory status, etc. All paramedics participating in the trial study will have received additional, specialized instruction in the use and interpretation of oxygen saturation monitors (pulse oximetry), indeed, most paramedics in San Diego County have already incorporated pulse oximetry into their assessment procedures. Base hospital radio personnel routinely use field oximetry data to refine the prehospital treatment plan for individual patients.

   System wide quality assurance/improvement monitoring has not demonstrated significant deficiencies in this area of monitoring.

   As proposed in the trial study, the decision as to which patients should receive NMB will be partly dependant on the field paramedics' ability to correctly calculate a Glasgow Coma Score (GCS) in the field. Paramedics are trained in a general manner to understand GCS calculations, but will require additional, specific training before the trial study to become proficient in this assessment. The training modules attached to this document include a proposed training module to increase the proficiency of EMT-Paramedics to correctly make an accurate and consistent GCS determination using a video presentation (using standardized patient scenarios) and skills demonstrations.

2. Patient treatment skills

   A. Venous access

   RSI requires that prehospital personnel have established a secure venous access for the patient. This fundamental skill is mandated within the California Scope of Practice for EMT-Paramedics.

   B. Hyper-oxygenation

   Hyper oxygenation with 100% oxygen via bag/valve/mask apparatus, or through the use of high flow mask is a skill already in use by EMT-Paramedics and EMT-1s throughout the prehospital care system. This is a basic skill for all prehospital certificate/license holders.

3. Medication administration.

All licensed paramedics demonstrate competency in calculating correct dosages of many medications based on weight, size, or standard criteria developed by the local EMS agency through the state's licensure process.

To minimize dosage errors, patients will be classified in the field by paramedics as either "Small" (35-63 Kg.), "Medium (64Kg-100Kg) or "Large"(>100Kg. Standardized dosages have been calculated for each of these approximate weight ranges (see field treatment protocol).

5. Endotracheal Tube placement (adult)
This skill is included in the State Scope of Practice for Paramedics. This skill has undergone intense scrutiny and quality improvement analysis, and paramedics continue to demonstrate that they can perform this procedure on the appropriate patients with reliability and skill.

Training will be designed and coordinated by the directors of the two approved EMT-P training agencies in San Diego County. The content, presentation and testing of necessary information will be developed by the training agencies and a field Advisory Committee, and shall be approved by the local EMS Medical Director.

Training modules and tests are still under development pending approval for the study, but outlines of proposed content are included in an attachment to this document. The behavioral objectives to be attained include the following:

1. The participant will demonstrate knowledge of the purpose, scope, ethics and EMT-P responsibilities involved in the study, as demonstrated verbally to an instructor and upon written examination.

2. The participant will demonstrate a thorough clinical knowledge of the medications used in the study (succinylcholine, rocuronium, midazolam), as demonstrated via written examination.

3. The participant will demonstrate, through written examination, awareness of proper storage measures and administration precautions to be taken for the medications used in the study.

4. The participant will demonstrate ability to calculate Glasgow Coma Score measurements by correctly calculating the score given standardized patient situations (perhaps via video)

5. The participant will be able to verbalize all components of the treatment protocol that will be utilized during the study.

6. The participant will demonstrate appropriate skill and judgement capabilities by successfully negotiating an Airway Mega-code exercise.

7. The participant will understand the mechanism by which the field paramedic will enter patient care data into the QA-Net for study evaluation, as demonstrated on the QA-Net to an instructor, and via written examination.

In the event that endotracheal intubation efforts remain unsuccessful for individual patients who have received NMB, field personnel (including some EMT-1 Defibrillation agency personnel) will be expected to attempt to position an esophageal-tracheal double lumen airway ("Combitube™") for improved airway control.

Attachments List

I. Research Protocol (prepared for presentation to Trauma Center Investigative Review Boards and Scope of Practice Committee).

Protocol Summary
Master Protocol
Treatment Protocol
Paramedic Data Worksheet
Standing Orders

II. Training Plan

III. Trauma Registry Complications List

IV. Letters of Support

V. Supporting Literature

Rapid Sequence Intubation - Protocol Summary

Protocol Title	Neuromuscular Blocking Agent Use by Field Paramedics in Endotracheal Intubation of Adult Trauma Patients with Glasgow Coma Scores of 8 or less
Study Objectives	Evaluate decrease in hypoxia-mediated secondary brain injury and improvement in success rates of intubation.
Primary Endpoints	pO_2 on arrival at Trauma Center pH on arrival at Trauma Center In-house complications during the first 30 days Glasgow Outcome Score at discharge, 3 months and 6 months Mortality
Subject Population	All adult trauma patients (≥ 18 years of age) with Glasgow Coma Score of 8 or less
Study Design	Prospective, matched cohort study
Study Medications	Midazolam (Versed), 5 mg/ml, 2 ml vials. Succinylcholine, 20 mg/ml, 10 ml vials. Rocuronium (Zemuron), 10 mg/ml, 5 ml vials. Morphine Sulfate, 10 mg/2ml
Dosage form	Sterile solution
Route of Administration	Intravenous
Dose and Regimen	Midazolam 3-5 mg IV for induction/amnesic effect if necessary, pre-intubation. Succinylcholine, 80 -160 mg IV (weight related dose) prior to intubation. Rocuronium, 40 mg - 80 mg IV (weight related dose) following successful intubation; repeated doses at 10-20 mg IV as needed for maintenance. Morphine sulfate, 2 mg IV, after intubation, for hypertensive stress response if heart rate is greater than 90/minute and BP is greater than 160 systolic. May be repeated every 3 minutes.
Duration of treatment	During field treatment and transport to trauma center.
Duration of Subject Participation in Study	Final Glasgow Outcome Score at 6 months.
Number of Evaluable Subjects Required to Meet Protocol Objectives	100 patients
Number of Study Centers	5 Trauma Centers (10-20 patients/Trauma Center/year)

Rapid Sequence Intubation - Master Protocol

Title

Neuromuscular Blocking Agent Use by Field Paramedics in Endotracheal Intubation of Adult Trauma Patients with Glasgow Coma Scores of 8 or less.

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Facilities

All patients treated in the field under the study protocol will be taken to Trauma Centers where outcome data will be collected. No treatment portion of the study will be carried out in the hospitals. The receiving facilities are:

UCSD Medical Center

Mercy Hospital Medical Center

Palomar Hospital Medical Center

Scripps Memorial Hospital, La Jolla

Sharp Memorial Hospital

Duration of the study

3 years (18 month study with anticipated 18 month continuation)

Specific Aims

1. Evaluate the effectiveness of neuromuscular blocking agents in improving prehospital intubation success rates in adults with severe head injury.

2. Evaluate the effectiveness of rapid sequence intubation by paramedics in the prehospital setting in preventing hypoxia related secondary brain injury based on clinical outcome measurements of:
   a. Hypoxia on admission
   b. Mortality
   c. Complications
   d. 3 and 6 month Glasgow outcome score

Background and Significance

Improvements in prehospital care over the past 25 years with rapid response and advanced airway management have resulted in increased survival rates and improved outcomes. While field treatment protocols aim at prevention of hypoxia in severely head injured patients by endotracheal intubation and controlled ventilation, analysis of intubation success rates in adult trauma patients with Glasgow coma scores of 8 or less show that intubation is successful in only 9% of patients with a GCS of 8, ranging up to 50% success in GCS of 3. (1)

Chesnut (2), et al, reviewed a large, prospectively collected data set from the Traumatic Coma Data Bank and demonstrated that hypoxia (apnea/cyanosis in the field or a PaO_2 < 60 mm Hg by arterial blood gas analysis) was among the 5 most powerful predictors of outcome, with hypoxia occuring in over 1/3 of the cases. A single instance of hypoxia was associated with a 42% mortality rate and of hypotension was associated with a 53% mortality. If neither was present, the mortality rate was 6%.

Winchell (3), et al, analyzed data from a 4 year period and showed that in 671 blunt trauma patients with severe head injury (GCS $\leq$ 8), those who were intubated in the field had a 37% improved survival (mortality 36% vs. 57%) compared to those who were not. In cases of isolated severe head injury, mortality fell from 50% to 23% with intubation.

Vilke (4), et al, has shown, in a review of 630 patients treated by aeromedical personnal that rapid sequence induction orotracheal intubation had a higher success rate, fewer complications, and a better patient outcome compared to noninduced orotracheal intubation and blind nasotracheal intubation.

It is postulated therefore, that by expanding the scope of practice of the paramedics to include use of neuromuscular blocking agents, we can improve intubation success, lessen the incidence of hypoxia and improve outcome by minimizing secondary brain injury.

References

1. Unpublished data. San Diego County QA net. Intubation success on trauma patients based on Glasgow Coma Score. 1/1/95 through 6/30/95.

2. Chesnut RM, Marshall LF, Klauber MR, et al: The role of secondary brain injury in determining outcome from severe head injury. J Trauma 34:216-222, 1993

3. Winchell RJ, Hoyt DB and Simons RK. Unpublished data. Abstract to be submitted to Western Surgical. 1996.

4. Vilke GM, Hoyt DB, Epperson M, et al. Intubation techniques in the helicopter. J Emerg Med 1994 Mar-Apr;12(2):217-24.

Research Design and Methods

Paramedics will be trained to perform Glasgow coma scores utilizing a video format with models demonstrating various response levels. There will also be a section in the video for testing performance and accuracy in determining GCS. The paramedics already are trained in the performance of endotracheal intubation and combitube intubation, however a brief refresher module will be included on the combitube which will be the back-up intubation device for failed orotracheal intubation. Training will also include modules on the pharmacology and physiologic effects of succinylcholine, rocuronium (zemuron) and midazolam (versed) which will be the agents used in the study. Emphasis will be placed on prevention of hypoxia and hypotension throughout the training module.

Field treatment will follow this protocol:

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Standing Orders for RSI Study:

Altered level of consciousness in Trauma Patients with a Glasgow Coma Score of 8 or less:

Adults appearing to be 18 years of age or older
IV NS TKO.
If hypotension present, treat per S-138 "Shock due to suspected hypovolemia" with bilateral IV NS wide open.
Document O_2 saturation by pulse oximetry.
Intubate and ventilate to establish oxygen saturation of 95%, then maintain ventilation at estimated tidal volume of 800 cc and ventilatory rate of 12 per minute.
In presence of any reactive resistance to intubation, if time interval to delivery of patient into Trauma Resuscitation suite is expected to be less than 10 minutes, transport immediately.
In presence of any reactive resistance to intubation, if time interval to delivery of patient into Trauma Resuscitation suite is expected to exceed 10 minutes:
Establish IV rate at 200 ml/hr
Midazolam 3-5 mg IV push per patient size.
Succinylcholine, 80 to 160 mg IV push per patient size:

Patient Size:	"Small"	"Average"	"Large"
Est. Weight - pounds	80-140	141-225	Over 225 (to 300)
-kilograms	35-63	63-100	>100 (to 135)
Dose Midazolam	**0.6 ml** (3 mg)	**0.8 ml** (4 mg)	**1.0 ml** (5 mg)
Dose Succinylcholine (Sux) in ml.:	**4 ml**	**6 ml**	**8 ml**
Dose Sux in mg. @ 20 mg/ml (approx 1.5 mg/kg)	80 mg	120 mg	160 mg
mg Sux/kg body wt.	2.3 - 1.3	1.9 - 1.2	1.6 - 1.2

Following all intubations with succinylcholine, or in the presence of reactivity (coughing, "bucking") to an endotracheal tube previously placed without use of succinylcholine give

Rocuronium 40-80 mg IV push per patient size.

Patient Size:	"Small"	"Average"	"Large"
Est. Weight - pounds	80-140	141-225	Over 225 (to 300)
-kilograms	35-63	63-100	>100 (to 135)
Dose Rocuronium in ml.:	**4 ml**	**6 ml**	**8 ml**
Dose Rocuronium in mg. @ 10 mg/ml	40 mg	60 mg	80 mg
mg Rocuronium/kg body wt. (0.6-1.2mg)	1.1 - 0.96	0.95 - 0.6	0.8 - 0.6

May repeat Rocuronium, 10-20 mg IV as needed for maintenance of neuromuscular blockade.

Patient Size:	"Small"	"Average"	"Large"
Est. Weight - pounds	80-140	141-225	Over 225 (to 300)
-kilograms	35-63	63-100	>100 (to 135)
Maintainance Dose Rocuronium in ml.:	**1.0 ml**	**1.5 ml**	**2.0 ml**
Dose Rocuronium in mg. @ 10 mg/ml	10 mg	15 mg	20 mg

Verify all endotracheal tube placements involving neuromuscular blocking agent use with:
Aspiration method (Toomey syringe or other suction based device), and
End-tidal CO_2 detection device (continuous), and
Pulse oximetry(continuous).

Following intubation and neuromuscular blockade, if heart rate is greater than 90 **and** blood pressure is greater than 160 systolic, give
Morphine sulfate 2 mg IV q 3 min as needed for stress response.
Repeat Midazolam 2 mg IV q 15 min to maintain amnesia unless BP is less than 120 systolic.

Transport destination: Trauma Center

Study Design

This is a cohort study. The historical cohort will be developed from Trauma Registry Database of 57,000 patients, matched for AIS for head injury, AIS for other body regions, ISS and age. This historical cohort will be preferentially drawn from the most recent cases in the Registry. The 100 patient study cohort and the 100 patient historical cohort will be expected to provide comparable samples of patients with hypoxia and hypotension, however, due to the demonstrated significance of these conditions in secondary brain injury, special analysis of these 2 conditions will be performed.

The results will be analzyed using a chi-square test at a significance of "p" = 0.05. For this level of significance, a sample of at least 100 patients will be collected from each cohort. One study cohort will be those who receive neuromuscular blocking agents prior to intubation. This sample will be compared to a historical cohort who were not intubated. Additionally another study cohort will be collected from those receiving neuromuscular blocking agents after successful intubation.

All prehospital traumatically injured adult patients with a GCS of 8 or less will be intubated in the field beginning 1 Jul 97. Mortality rate and as well as rate of complications listed in the Trauma Registry for the patients intubated with, or subsequently receiving, neuromuscular blocking agents will be compared to the cohort of patients who were not intubated, and will be matched for AIS for head injury, AIS for other body regions, ISS and age.

Of these patients, those subsequently determined not to have internal head injury will be excluded from that analysis, but will be tracked and analyzed for cause of altered neurologic status, such as drugs, alcohol, metabolic factors, etc. These patients will also be tracked for mortality and complications. This cohort will be analyzed for mortality and complications against the Trauma Registry database cohort, matched for AIS for body regions, ISS and age.

All prehospital patients receiving neuromuscular blocking agents who have failed intubation will be tracked and analyzed. Mortality rate and as well as rate of complications listed in the Trauma Registry for these patients will be compared to a cohort of patients who were not intubated, and will be matched for AIS for head injury, AIS for other body regions, ISS and age.

While mortality rate is the primary measure, rate of listed complications will also be compared and studied. In addition, Dr. Larry Marshall, professor and head of neurosurgery at UCSD, will review all the CT scans on the head injured treated patients, will arrange for his

neurosurgical research nurses to perform the Glasgow outcome score at 3 and 6 months on the study patients and will compare outcomes to matched controls from the 2000 patient severe-head injury data base that has been developed under the international drug studies on tirilazad (Upjohn) and selfotel (Ciba) for which he has been the international study center coordinator. The results will be analzyed using a chi-square test at a significance of "p" = 0.05.

ALL DATA COLLECTION WILL BE MANAGED IN A CONFIDENTIAL MANNER, USING UNIQUE NUMERICAL PATEINT IDENTIFIERS, NOT PATIENT NAMES.

San Diego County Emergency Medical Services
Trial Study Proposal
Neuromuscular Blockers & Advanced Sedation

(This worksheet will be used to capture data on all study patients, documenting field treatment as well as data points on arrival at the trauma center.)

San Diego County Neuromuscular Blockade Study - Paramedic Worksheet

QANet Record #: _____ Inpatient ID #: _____
Agency: _____ Unit#: _____
Date of Incident: _____ Time of Incident (approx): _____

INITIAL PHASE - Assessment
Initial BP: ____ / ____ Initial Pulse: _____ Initial Resp rate: _____
Cyanosis **Y / N** Initial O2 Sat: _____ Pt Age: _____ (≥ =18)
Initial GCS-Eye:____ Verbal: _____ Motor: _____ Total: _____ (≤ =8)
ET intubation attempted prior to NMB consideration? **Y / N** Successful? **Y / N**
Estimated elapsed time to delivery of pt. to trauma resus room: ____ min (≥10 min)
PRIMARY Indication to use NMB: □clenched teeth □blood/vomit □unmanageable
Is there indication that the patient has aspirated? **Y / N**
Time decision to use NMB made: _____

MEDICATIONS - Initial NMB dosage (circle doses given)

Patient Weight	35-63 Kg 80-140 lbs.	63-100 Kg 141-225 lbs	>100 Kg >225 lbs	Time of dose
Midazolam	3 mg. =0.6cc	4 mg. = 0.8cc	5 mg. =1.0cc	
Succinylcholine	80 mg = 4 cc	120 mg = 6 cc	160mg =8cc	

Continue ventilatory support.

INTUBATE, CONFIRM ET TUBE PLACEMENT □Observation □Toomey □ETCO2 □Auscultation
ET Successful? **Y / N** (#of attempts ___) If no, attempt Combitube-Successful? **Y / N**, # attempts ___)
Any indication that patient may have vomited or aspirated during intubation procedure? **Y / N**

Rocuronium	40 mg = 4 cc	60 mg = 6 cc	80mg =8 cc	
Morphine Sulfate (BP> =160/x),HR> =90	2 mg	2 mg	2 mg	

VENTILATE 100% O2 to bring O2 Sat to ≥95, then 800cc TV X 12/min

PATIENT BECOMES UNMANAGEABLE post Intubation? - **No NMB yet?**

Midazolam	3mg = 0.6cc	4mg = 0.8cc	5mg = 1.0cc	
Rocuronium	40 mg = 4 cc	60 mg = 6 cc	80mg = 8 cc	

REPEAT ROCURONIUM prn - movement (increased spontaneous respiratory activity ,"bucking", gagging, etc.)

10 mg = 1cc	15 mg = 1.5 cc	20mg = 2cc	

REPEAT MIDAZOLAM Q 15 MINUTES

2 mg = 0.4 cc	2 mg = 0.4 cc	2 mg = 0.4 cc	
2 mg = 0.4 cc	2 mg = 0.4 cc	2 mg = 0.4 cc	

DELIVERY TO TRAUMA RESUS ROOM
Time of arrival to resus room _____ Last O2 sat;_____ Pt still flaccid? **Yes / No**
Resus Room Outcome (if known) □OR □ICU □ Expired □ Other _____

SPECIAL NOTES, EXPLANATIONS
Physician variations from this research protocol are prohibited!
double underlined parameters are mandatory requisites for study

Initial BP = BP measured immediately prior to RSI
Initial O_2 sat = O_2 sat measured immediately prior to RSI

	Eye Opening	Verbal Response	Motor Response
6			Obeys Command
5		Oriented	Localizes Pain
4	Spontaneous	Confused	Withdraw from Pain
3	To Voice	Inapp Words	Flexion to Pain
2	To Pain	Incomp Words	Extension to Pain
1	None	None	None

Base hospital contact must be made as soon as possible during encounter to enroll patient into study

This worksheet must be delivered with patient to the receiving facility.

Complete QANet documentation must be completed by field personnel upon delivery of patient to ED. GCS Scale

*****

Data collection at the Trauma Center will include incidence of complications (see listings in the attachment section of this document) and mortality and Glasgow outcome score at 3 and 6 months with evaluation carried out by neurosurgical research nursing staff.

While ideally this study would be carried out like many other field trial studies, utilizing an alternate day methodology, the compelling nature of available data on the impact of airway on outcome and mortality made this ethically unjustifiable. The next most valid technique using a prospective, matched cohort study methodology was selected.

Each study patient will be case controlled from the 57,000 patients existing in the trauma registry data base, matched for ISS, age, AIS for head injury, and AIS for other body regions.

Attachment II -

General Student Training Objectives

1. The participant will demonstrate knowledge of the purpose, scope, ethics and EMT-P responsibilities involved in the Study, as demonstrated verbally to an instructor and upon written examination.

2. The participant will demonstrate a thorough clinical knowledge of the medications used in the study (succinylcholine, rocuronium, midazolam), as demonstrated via written examination.

3. The participant will demonstrate, through written examination, awareness of proper storage measures and administration precautions to be taken for the medications used in the study.

4. The participant will demonstrate ability to calculate Glasgow Coma Scale measurements by correctly calculating the score given standardized patient situations (perhaps via video)

5. The participant will be able to verbalize all components of the treatment protocol that will be utilized during the study.

6. The participant will demonstrate appropriate skill and judgement capabilities by successfully negotiating an Airway Mega-code exercise.

7. The participant will understand the mechanism by which the field paramedic will enter patient care data into the QA-Net for study evaluation, as demonstrated on the QA-Net to an instructor, and via written examination.

Training Overview - Training Day - NMB Project

I. Homework - Prior to the scheduled class, each student will receive an information packet with training materials covering the basic didactic information necessary for the paramedic participating in the project. This packet will include such materials as

A. Drug sheets for study medications. Actions, Indications, Contraindications, Dosages.
B. Study Treatment Protocol

II. At the beginning of the scheduled training day, the student will take a challenging pre-test which measures competency in the information presented in the "homework" - students who pass the pre-test shall be awarded 3 hours continuing education credit and will be permitted to participate in the rest of the day's training. Students who fail the pretest will be awarded no CE credit and will be rescheduled to take the training at another time.

III. The training day will consist of a series of standardized training sessions.

A. Pretest. Registration, etc. (1/2 hour)
B. Overview of Study - implications for paramedics, legal/ethical considerations, importance of critical thinking, etc. (1/2 hour)
C. Glasgow Coma Scale video, including testing on standardized patient situations (1 hour)
D. Airway review - Basic airway techniques, Combitube, ET intubation (demo?) etc. (1 hour)
E. Drug/Protocol Review (1/2 hour)
F. Study Requirements - Data collection and reporting, patient eligibility, what ifs..., (1/2 hour)
G. Airway Mega-code - Demonstration (1 hour)
H. Post-test (1/2 hour)

The Airway Mega-code demonstration will use a minimum instructor:student ratio of 1:6.

The individual who successfully completes the day's training will receive an additional 6 hours CE credit

Notes:
1. Training will be limited to trainers from approved EMT-P training programs and educators from base hospital operations
2. Training standards for Mega-Code demand 1:6 teacher:student ratio.

PREHOSPITAL - Airway
==========
1001 Aspiration/Pneumonia
1002 Esophageal Intubation
1003 Extubation, Unintentional
1004 Mainstem Intubation
1005 Unable to intubate
1099 Other

PREHOSPITAL - Fluids
==========
1501 Inappropriate fluid management
1502 Unable to start an IV
1599 Other

PREHOSPITAL - Miscellaneous
==========
2001 No EMS form
2002 Incomplete EMS form
2003 Prehospital delay
2080 Triage
2099 Other prehospital

HOSPITAL - Airway
==========
2501 Esophageal Intubation
2502 Extubation, Unintentional
2503 Mainstem Intubation
2599 Other airway

HOSPITAL - Pulmonary
==========
3001 Abscess
3002 ARDS
3003 Aspiration/pneumonia
3004 Atelectasis
3005 Empyema
3006 Fat embolus
3007 Hemothorax
3008 Pneumonia
3009 Pneumothorax (barotrauma)
3010 Pneumothorax (iatrogenic)
3011 Pneumothorax (recurrent)
3012 Pneumothorax (tension)
3013 Pulmonary edema
3014 Pulmonary embolus
3015 Respiratory failure/distress
3016 Upper airway obstruction
3017 Pleural effusion
3099 Other pulmonary

HOSPITAL - Cardiovascular
==========
3501 Arrhythmia
3502 Cardiac Arrest (unexpected)
3503 Cardiogenic Shock
3504 CHF (iatrogenic)
3505 MI
3506 Pericarditis
3507 Pericardial Effusion or Tamponade
3508 Shock
3599 Other cardiovascular

HOSPITAL - GI
==========
4001 Anastomotic Leak
4002 Bowel injury (iatrogenic)
4003 Dehiscence/+Evisceration
4004 Enterostomy
4005 Fistula
4006 Hemorrhage - lower GI
4007 Hemorrhage - upper GI
4008 Ileus
4009 Peritonitis
4010 SBO
4011 Ulcer - duodenal/gastric
4099 Other GI

HOSPITAL - Hepatic/Biliary
==========
4501 Acalculous Cholecystitis
4502 Hepatitis
4503 Liver Failure
4504 Pancreatic fistula
4505 Pancreatitis
4506 Splenic Injury (iatrogenic)
4599 Other hepatic/biliary

HOSPITAL - Hematologic
==========
5001 Coagulopathy (intraop)
5002 Coagulopathy (other)
5003 DIC
5004 Serum sodium >160 (peds only)
5005 Transfusion complication
5099 Other hematologic

HOSPITAL - Infection
==========
5501 Cellulitis/traumatic injury
5502 Fungal sepsis
5503 Intra-abdominal Abscess
5504 Line infection
5505 Necrotizing fascitis
5506 Sepsis-like syndrome
5507 Septicemia
5508 Sinusitis
5509 Wound infection
5510 Yeast infection
5599 Other infection

HOSPITAL - Renal
==========
6001 Renal failure
6002 Ureteral Injury
6003 UTI, early
6004 UTI, Late
6099 Other renal/GU

HOSPITAL - MUSCULOSKELETAL/INTEGUMENTARY
==========
6501 Compartment Syndrome
6502 Decubiti Grade minor
6503 Decubiti Grade blister
6504 Decubiti Grade open sore
6505 Decubiti Grade deep
6506 Loss of Reduction/fixation
6507 Non union
6508 Osteomyelitis
6509 Orthopedic wound infection
6599 Other

HOSPITAL - Neurologic
==========
7001 Alcohol withdrawal
7002 Anoxic Encephalopathy
7003 Brain death
7004 Diabetes Insipidus
7005 Meningitis
7006 Neuropraxia (iatrogenic)
7007 Non-operative SDH/EDH
7008 Progression of Original Neurologic Insult
7009 Seizure
7010 SIADH
7011 Stroke/CVA
7012 Ventriculitis - post surgical
7099 Other neurologic

HOSPITAL - Vascular
==========
7501 Anastomosis Hemorrhage
7502 DVT (lower extremity)
7503 DVT (upper extremity)
7504 Embolus (non pulmonary)
7505 Gangrene
7506 Graft Infection
7507 Thrombosis
7599 Other vascular

8001 Psych

HOSPITAL - Other
==========
8501 Anesthetic Complication
8502 Drugs
8503 Fluids
8504 Hypothermia
8505 Monitoring
8506 Return to OR
8507 Unexpected Readmission
8508 Unexpected Post-operative Hemorrhage
8509 Abdominal Non-Op Management
8510 Managed Care Issue
8599 Other

HOSPITAL - Errors/Delays
==========
9002 Delay in Trauma Team activation
9003 Delay to Operating Room
9004 Delay in MD response
9005 Delay in obtaining consult
9006 Delay in diagnosis
9007 Error in diagnosis
9008 Error in judgement
9009 Error in technique
9010 Incomplete Hospital Record
9011 Delay in Trauma Consult
9012 Delay in Presentation (acceptable by definition)

NOTE: Italics indicate July 1, 1995 changes

March 19, 1996

Joseph Morales, M.D.
Director
State Emergency Medical Services Authority
1930 Ninth Street, Suite 100
Sacramento, CA 95814-7043

Dear Dr. Morales:

On behalf of the San Diego Trauma System, we the trauma directors request response to the recent proposed study for head injured patients being served with field intubation by the paramedics in San Diego County.

We have well-documented evidence that at least 150 or more patients will be affected by this in San Diego County. Further, we have spent much time interacting with the neurosurgery community, including some of their national leaders, to arrive at the following conclusion: this subgroup of patients who has sustained head injury and whom prehospital airway maintenance is not secured can have potentially devastating effects of superimposed hypoxia. For this reason, training paramedics in prehospital airway control is justified. If one were to translate this to the number of patients potentially affected on a national level, it would be equivalent to approximately 15,000 patients nationwide. This is almost equal to the incidence of severe spinal injuries nationwide.

We would request that you outline your concerns as to why a proposed prospective study is not appropriate or immediately see that this is approved so that we can proceed with this essential research. Please let us know at your earliest convenience.

Sincerely,

David B. Hoyt, M.D.
Chief, Division of Trauma
UCSD Medical Center

Michael J. Sise, M.D.
Trauma Director
Mercy Healthcare San Diego

A. Brent Eastman, M.D.
Trauma Director
Scripps Memorial Hospital

Timothy G. Carey, M.D.
Trauma Director
Children's Hospital and Health Center

Thomas Wachtel, M.D.
Trauma Director
Sharp Memorial Hospital

Thomas Velky, M.D.
Trauma Director
Palomar Medical Center

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CYNDI M. POPE
CLINICAL COORDINATOR

October 16, 1996

Mel A. Ochs, M.D., FACEP
Medical Director
Division of Emergency Medical Services
6255 Mission Gorge Road
San Diego, CA 92120-3599

RE: Rapid Sequence Intubation

Dear Mel:

I have reviewed this and, in general, I think it is very good. Some greater details regarding how the case control methodology could be utilized would be helpful, particularly for the skeptical observer who will adhere to the desire for a classic randomized clinical trial. We would be glad to help you get this going.

My best wishes as always.

Sincerely yours,

Written, not read

Lawrence F. Marshall, M.D.
Professor and Chair,
Division of Neurological Surgery
University of California, San Diego Medical Center

LFM/ldr

BASE STATION PHYSICIANS COMMITTEE

OF SAN DIEGO COUNTY

MARK KRAMER, M.D., CHAIRMAN
BASE STATION PHYSICIANS' COMMITTEE
c/o SHARP MEMORIAL HOSPITAL
7901 FROST STREET
SAN DIEGO, CA 92123-2784

November 5, 1996

Joseph Morales, M.D.
Director
EMS Authority
1930 9th Street, Suite 100
Sacramento, CA 95814

Dear Dr. Morales:

The Base Station Physicians' Committee of San Diego County strongly supports the County EMS proposal to study the use of RSI in trauma patients with Glasgow Coma Score of eight or less. The use of this advanced pharmacologic technique in EMS has stirred great debate but has not been studied to date in a rigorous way. By studying this group of RSI trauma patients and matching their "outcomes" to a cohort of patients chosen from San Diego Trauma Registry data, it is our hope to provide data that will resolve the question of efficacy for the use of RSI in Trauma-EMS. The study will enroll 100 patients over three years and will involve active support from UCSD Trauma and Neurosurgery Services.

The Base Station Physicians' Committee has been intensively developing and studying county airway data for two years and has been interested in methods that increase EMS' ability to control airways in trauma patients with Glasgow Coma Scores of eight or less. Strong support from the County Trauma System led us to encourage this study that will specifically address outcome data. The study is well designed, it has broad based support within the County EMS and Trauma Communities, and this Committee strongly supports its approval.

Sincerely,

Mark J. Kramer, M.D.

MARK J. KRAMER, M.D., Chairperson
Base Stations Physicians' Committee

MJK:tb
cc: Scope of Practice Committee
San Diego County EMS Agency

FYI - A Copy of letter sent to Dr. Morales. Todd K.

SDCPA

San Diego County Paramedic Association
P.O. Box 232202
San Diego, CA 92193

March 25, 1996

Dear Dr. Morales,

This letter is in regard to the recently proposed Rapid Sequence Induction- RSI study that is to begin in San Diego County. It is the feeling of this Association that RSI would be a major benefit to patients in the pre-hospital setting. The decision to pursue this regiment was clearly thought out involving many San Diego EMS professionals and outside experts as well. The ongoing efforts by our local EMS agency to further validate and research this topic in order to gain State approval is commendable and we hope it will convince those involved of the appropriateness of this study.

Delivering oxygen to our patients is a Paramedics most important duty. This treatment is often constrained by environmental factors that require effort to overcome. Combative patients with ineffective respirations or those with clenched down and otherwise unmanageable airways work only to compound the problem of oxygen delivery. With the availability of RSI the often disastrous progression of these patients could be reversed and the inept struggle to manage their compromised airways would be eliminated. San Diego EMS has clearly identified this at risk population statistically and at long last agreed to treat them as the standard of care indicates. This standard is RSI and it is commonly used in Emergency Departments, Trauma Centers, aero medical operations and by selected pre-hospital ALS personnel. It is our position that patients deserve the standard of care whenever practical, and it has been demonstrated practical for Paramedics to deliver RSI. Paramedics are highly successful in skills application, especially intubation, even in austere conditions. Careful medication administration is nothing new for field personnel and it has always demanded high levels of knowledge. With all this in mind it would be justified to allow this treatment, especially when balanced against the likely outcome if RSI is not enacted and an airway is never secured.

The indications are clear and complications must be considered. Blind nasal tracheal intubation-NTI has long been in the State scope of practice for Paramedics. Unfortunately it is not the indicated treatment for the populations identified for this study. Also more complications are being seen with this method of intubation than with RSI. A lengthy study by Life Flight in San Diego has supported this as have other studies. The superiority of RSI makes it the ideal tool for Paramedics due to its short - rapid action. Clinical settings are prepared to administer a surgical airway in the face of failed or complicated intubations. If this rare situation is a concern for field use of RSI then agencies may want to locally implement the use of needle crichothyroidostomy, which all California Paramedics are trained to administer under the State scope of practice guidelines.

San Diego is an ideal location for this study to begin. It is Americas sixth largest city that combines every EMS environment from urban to rural. EMT-D Responders are highly skilled and have now begun utilizing the Combitube to further protect patients airways. Paramedics here use strict criteria for proper ET tube placement that include esophageal aspiration devices and end tidal CO2 detectors. San Diego County will also be fully computerized for data collection in the near future.

Our local Association has long been a proponent of this life saving technique. The motivation for this comes strictly from a patient care perspective. Although we feel strongly that this will help a great deal of patients it will also help many Paramedics to feel good about the rescue efforts they have made. There are too many Paramedics with memories of powerlessness in trying to care for patients dying due to a potentially correctable airway problem. We are asking to be given a chance to serve our patients and for these patients to be given their best chance for survival. We at the SDCPA strongly encourage you to lead the way in this move to provide the proven standard of care to those that need it most, the pre-hospital patient.

Sincerely,

Todd J. Klingensmith

Todd J. Klingensmith
SDCPA President
Phone (619)445-0425

P.S. Enclosed is a recent newsletter article on the same subject, thank you for your time.

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THE ROLE OF SECONDARY BRAIN INJURY IN DETERMINING OUTCOME FROM SEVERE HEAD INJURY

Randall M. Chesnut, MD,[a,b] Lawrence F. Marshall, MD,[a] Melville R. Klauber, PhD,[c] Barbara A. Blunt, MPH,[c] Nevan Baldwin, MD,[d] Howard M. Eisenberg, MD,[e] John A. Jane, MD,[f] Anthony Marmarou, PhD,[d] and Mary A. Foulkes PhD[g]

As triage and resuscitation protocols evolve, it is critical to determine the major extracranial variables influencing outcome in the setting of severe head injury. We prospectively studied the outcome from severe head injury (GCS score ≤ 8) in 717 cases in the Traumatic Coma Data Bank. We investigated the impact on outcome of hypotension (SBP < 90 mm Hg) and hypoxia ($Pao_2 \leq 60$ mm Hg or apnea or cyanosis in the field) as secondary brain insults, occurring from injury through resuscitation. Hypoxia and hypotension were independently associated with significant increases in morbidity and mortality from severe head injury. Hypotension was profoundly detrimental, occurring in 34.6% of these patients and associated with a 150% increase in mortality. The increased morbidity and mortality related to severe trauma to an extracranial organ system appeared primarily attributable to associated hypotension. Improvements in trauma care delivery over the past decade have not markedly altered the adverse influence of hypotension. Hypoxia and hypotension are common and detrimental secondary brain insults. Hypotension, particularly, is a major determinant of outcome from severe head injury. Resuscitation protocols for brain injured patients should assiduously avoid hypovolemic shock on an absolute basis.

A DECADE AGO, Miller et al. published the first detailed studies of the prevalence and significance of secondary systemic insults in 225 prospective patients at the Medical College of Virginia (MCV).[1-3] These patients came directly or were transferred to the MCV hospital because of head injury and met the criteria for admission to the study if they were unable to speak and obey commands (Table 1). It is apparent that hypoxia and hypotension were associated with a doubling of the mortality from severe head injury in this sample. Their operational definition of hypoxia was a $Pao_2 < 60$ mm Hg. Hypotension was defined as a systolic blood pressure (SBP) < 95 mm Hg. These values were recorded initially in the trauma center and do not represent events that resolved before patients reached the hospital. Note that their categories were not mutually exclusive (i.e., the category of hypoxia included patients who also incurred a hypotensive episode and vice versa).

We have used the data from the Traumatic Coma Data Bank (TCDB) to reinvestigate the findings of the MCV group to further clarify the role of secondary insults. We analyzed hypoxia and hypotension as four mutually exclusive categories: neither hypotension nor hypoxia, hypoxia only, hypotension only, and hypoxia and hypotension combined. We also attempted to control for other factors, age and severe multiple trauma in particular, that may interact with secondary insults to determine the independent influence of hypoxia and hypotension on outcome.

MATERIALS AND METHODS

The TCDB is a National Institute of Neurological Diseases and Stroke (NINDS) collaborative project involving four clinical centers, the Medical College of Virginia (MCV) at Richmond, the University of California at San Diego (UCSD), the University of Virginia (UVA) at Charlottesville, and the University of Texas Medical Branch (UTMB) at Galveston, with a coordinating center within the Biometry and Field Studies Branch, NINDS. These clinical centers prospectively studied all patients with severe head injuries admitted between April 1983 and April 1988. The operational definition of severe head

From the [a]Division of Neurological Surgery, UCSD Medical Center, San Diego, California and [b]Division of Neurological Surgery, San Diego Veterans Administration Hospital, La Jolla, California, the [c]Department of Community and Family Medicine, UCSD Medical Center, San Diego, California, the [d]Medical College of Virginia, Richmond, Virginia, the [e]University of Texas Medical Branch, Galveston, Texas, the [f]University of Virginia School of Medicine, Charlottesville, Virginia, and the [g]National Institute of Neurological Disorders and Stroke, Bethesda, Maryland.

This work was supported by the Traumatic Coma Data Bank (TCDB) under Contracts NO1-NS-3-2339, NO1-NS-3-2340, NO1-NS-3-2341, NO1-NS-3-2342, NO1-NS-6-2305 from the National Institute of Neurological Disorders and Stroke (NINDS). The TCDB Manual of Operations, which includes the TCDB data forms, is available from the National Technical Information Service (NTIS), U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161 (NTIS Accession No. PB87 228060/AS).

Part of this work was presented to the International Congress of Neurosurgical Societies in New Delhi, India, October, 1989 in receipt of the Volvo Award for Neurotrauma Research.

Address for reprints: Randall M. Chesnut MD, Division of Neurological Surgery H-893, 225 Dickinson St., University of California, San Diego Medical Center, San Diego, CA 92103-1990.

V-1

Table 1
Data from the Medical College of Virginia (1982)*: Outcome by secondary insult at time of arrival at hospital for non-mutually exclusive insults

Secondary Insults	Number of Patients	Percentage of Total Patients	Outcome Percentage		
			Good or Moderate	Severe or Vegetative	Dead
Total cases	225	100	56	10	34
Neither	120	53	64	12	24
Hypoxia	78	35	41	9	50
Hypotension	34	15	35	12	53

Hypoxia = $Pao_2 < 60$ mm Hg; hypotension = SBP < 95 mm Hg.
* Reprinted from Miller JD, Becker DP: Secondary insults to the injured brain. *J R Coll Surg Edinb* 27:292, 1982. With permission.

injury was a Glasgow Coma Scale (GCS)[4] score of 8 or less occurring on admission (postresuscitation) or during the ensuing 48 hours. In addition to data for the acute care course, prehospital information and rehabilitation follow-up results were collected. Patient outcome was determined by the last recorded Glasgow Outcome Scale (GOS) score.[5] The median time from injury to last recorded GOS score for survivors was 521 days, with a range of 5–1255 days.

The records of 1030 patients were included in the TCDB. Of these, 284 patients were brain dead on admission, did not survive resuscitation, or suffered a gunshot wound to the brain, leaving 746 patients. In 29 information on the prehospital course was insufficient to allow assessment, leaving 717 patients. Of these, 18 patients lacked initial blood pressure or arterial blood gas measurements from their time of arrival at the TCDB hospital. Therefore the present report analyzes the course of 717 patients from injury through resuscitation at the TCDB hospital emergency room and 699 patients for the time of arrival at the TCDB hospital emergency room.

For our studies, the operational definition of hypotension was a systolic blood pressure (SBP) $\leq$ 90 mm Hg. Hypoxia was defined as a $Pao_2 \leq 60$ mm Hg or as definite apnea or cyanosis in the field reported by Advanced Trauma Life Support (ATLS)-trained EMS personnel.

All injuries were classified using the Abbreviated Injury Scale (AIS).[6] This scale ranges from 1 to 6, with 1 being trivial and 6 almost uniformly fatal. Under this system, injuries graded 4 and greater are severe injuries. We subdivided the patients in each secondary brain insult category by the presence or absence of a concomitant severe injury (AIS grade greater than 3) to the neck, thorax, diaphragm, abdomen, pelvis, extremities, or spine. Patients with such injuries were classified as having severe multiple injuries and those without were classified as lacking severe multiple injuries.

The independence of individual secondary brain insults, age, and severe multiple injuries in determining outcome trends was analyzed using the extended Mantel-Haenszel (M-H) chi-square test.[7] Age was controlled in the M-H procedure by using two groups: 0–39 years of age, and 40 years of age and over. For summary purposes, the GOS score was collapsed from five to three categories in the tables; however, statistical testing using the GOS was performed using the full five-point scale. Log-linear models were used to analyze 2 × 2 × 2 contingency tables.[8] Homogeneity of a relationship between categories of patients (controlling for hypoxia, hypotension, and severe multiple trauma) was tested using interaction terms in polychotomous logistic regression models.[9] The 5% level was used to define statistical significance.

RESULTS

For the TCDB cohort of 717 patients, the median age was 25 years, with a range of 16 days to 93 years. Thirty-seven percent of patients fell into the 15–24-year age group. The ratio of males to females was 3.4:1. The median initial GCS score was 4, indicating a patient population weighted toward the more severely injured end of the scale. Sixty-one percent of patients were injured in motor vehicle crashes. Thirty-eight percent of patients were transfers to the TCDB hospital, having been seen initially at another institution. The median transport time from injury to the receiving hospital was 0.9 hours, with a mean ± SD of 1.3 ± 1.8 hours. Twenty-eight percent of these patients required craniotomy as a result of their head trauma.

Data from the TCDB are presented in Table 2 in the format used by Miller et al., employing non-mutually exclusive categories of hypoxia and hypotension and encompassing only the time of admission to the hospital. Comparison of Tables 1 and 2 confirms the findings of Miller and Becker by demonstrating the significant impact of secondary insults on the morbidity and mortality of brain injury in the TCDB patient cohort. Row-by-row comparison of Tables 1 and 2 for the categories of neither insult, hypotension, and hypoxia reveals no statistically significant differences in outcome trends between the two studies.

Hypoxia and Hypotension

In the analysis presented in this section, we controlled for age and severe multiple trauma. Discussion of the details of this analysis and of the individual influences of these factors is presented separately later.

We analyzed the TCDB data further by separating hypoxia and hypotension into mutually exclusive categories. Table 3 presents the data of Table 2, except that in Table 3 there is no overlap between the categories of hypoxia and hypotension. This analysis of mutually exclusive categories reveals that the major determinant of the overall increased morbidity and mortality resulting from secondary insult appears to have been hypotension.

Table 2
TCDB data: Outcome by secondary insult at time of arrival at TCDB hospital ER for non-mutually exclusive insults

Secondary Insults	Number of Patients	Percentage of Total Patients	Outcome Percentage		
			Good or Moderate	Severe or Vegetative	Dead
Total cases	699*	100.0	42.9	20.5	36.6
Neither	456	65.2	51.1	21.9	27.0
Hypoxia	130	18.6	29.2	20.8	50.0
Hypotension	165	23.6	19.4	15.8	64.8
Both	52	7.4	5.8	19.2	75.0

Hypoxia = $Pao_2 < 60$ mm Hg; hypotension = SBP < 90 mm Hg.
* The total number of patients is 699 instead of 717 because of missing admission data on blood pressure or arterial blood gas values in 18 patients.

Table 3
TCDB data: Outcome by secondary insult at time of arrival at TCDB hospital ER for mutually exclusive insults

Secondary Insults	Number of Patients	Percentage of Total Patients	Outcome Percentage		
			Good or Moderate	Severe or Vegetative	Dead
Total cases	699*	100.0	42.9	20.5	36.6
Neither	456	65.2	51.1	21.9	27.0
Hypoxia	78	11.2	44.9	21.8	33.3
Hypotension	113	16.2	25.7	14.1	60.2
Both	52	7.4	5.8	19.2	75.0

Hypoxia = $Pao_2 < 60$ mm Hg; hypotension = SBP < 90 mm Hg.
* The total number of patients is 699 instead of 717 because of missing admission data on blood pressure or arterial blood gas values in 18 patients.

Table 4
TCDB data: Outcome by secondary insult from time of injury through resuscitation at TCDB hospital ER for mutually exclusive insults

Secondary Insults	Number of Patients	Percentage of Total Patients	Outcome Percentage		
			Good or Moderate	Severe or Vegetative	Dead
Total cases	717	100.0	43.0	20.2	36.8
Neither	308	43.0	53.9	19.2	26.9
Hypoxia	161	22.4	50.3	21.7	28.0
Hypotension	82	11.4	32.9	17.1	50.0
Both	166	23.2	20.5	22.3	57.2

Hypoxia = $Pao_2 < 60$ mm Hg; hypotension = SBP $\leq$ 90 mm Hg.

Analysis of the association of outcome with hypotension controlled for hypoxia, age, and severe multiple trauma reveals that it was extremely significant ($p < 10^{-6}$). The association of outcome with hypoxia controlled for hypotension, age, and severe multiple trauma was also significant ($p = 0.001$). The detrimental impact of the combination of hypoxia and hypotension was significantly greater than that of hypotension alone ($p = 0.021$).

To more completely evaluate the frequency of occurrence and impact of hypoxia and hypotension on outcome, their prevalence and effects were evaluated for the expanded time interval from injury through resuscitation. Employing mutually exclusive categories for hypoxia and hypotension for this time period, Table 4 demonstrates the dominant role of hypotension with or without hypoxia in accounting for the morbidity and mortality of secondary insults. Analysis of the association of outcome with hypotension controlled for hypoxia, age, and severe multiple trauma in this cohort again reveals hypotension to have been extremely significant ($p < 10^{-6}$). Analysis of the independent association of outcome with hypoxia was also significant ($p = 0.013$). When one observes outcome based on secondary insults occurring in the longer time period, however, the effect of hypoxia appeared to diminish (compare Tables 3 and 4).

Also notable from these data is the frequency of occurrence of secondary insults. Table 4 demonstrates that hypoxia occurred in 45.6% of patients and hypotension in 34.6% of patients when the expanded time period from injury to arrival was examined.

Age

Outcome data by secondary brain insult from Tables 3 and 4 are presented in Figures 1 and 2 stratified by age. Patients less than 40 years old are presented in the upper graphs and those 40 years or greater are shown in

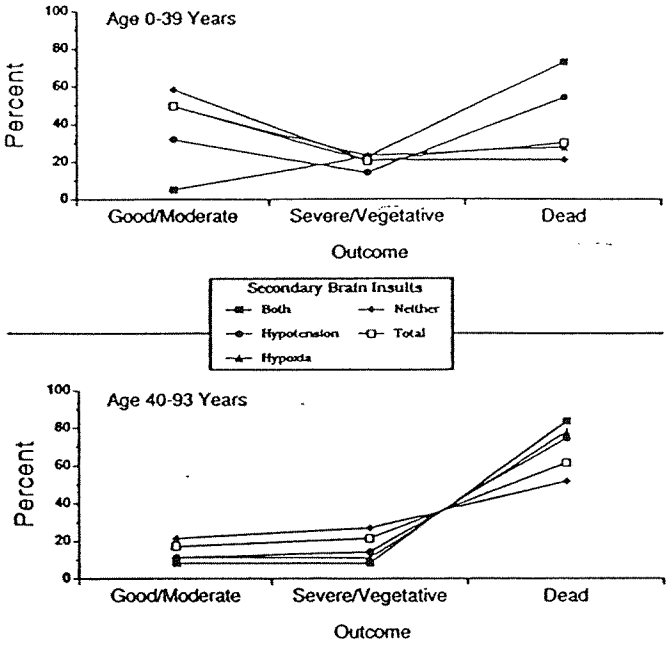

Figure 1. TCDB Data: Outcome by secondary insult at time of arrival at TCDB hospital ER for mutually exclusive insults by age (n = 699).

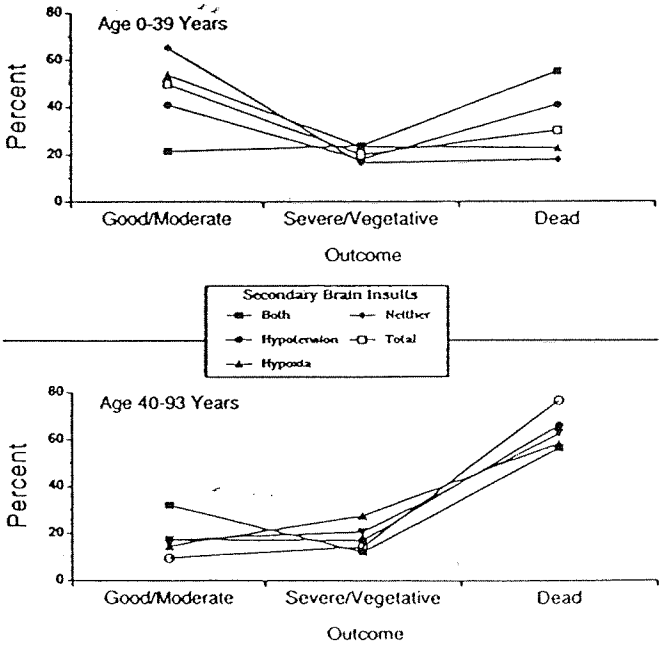

Figure 2. TCDB Data: Outcome by secondary insult from time of injury through resuscitation at TCDB hospital ER for mutually exclusive insults by age (n = 717).

the lower graphs. Figure 1 is for data collected at the time of arrival at the TCDB hospital. Figure 2 displays data for the expanded time period from injury through resuscitation.

Both Figures 1 and 2 have the appearance of a stronger association of hypoxia and hypotension with outcome for younger versus older patients. For the interaction of age and *hypotension*, polychotomous logistic regression showed no significant interaction using the data at either hospital admission or the extended time period. There was no significant difference in the strength of the association between hypotension and outcome for the two age groups.

For the interaction of age and *hypoxia*, there was also no significant difference in the strength of the association between *hypoxia* and outcome by age group for the data at hospital admission (Fig. 1). For this time period, therefore, the significant interaction between hypotension or hypoxia and outcome was not significantly age dependent.

The situation is different for the extended time period (Fig. 2). Here, polychotomous logistic regression showed a significant age-related difference in the strength of the association between hypoxia and outcome. We therefore repeated the Mantel-Haenszel analysis of this data partitioned by age group. This demonstrated that the association between hypoxia and outcome was composed of a highly significant association for the younger age group ($p = 0.0018$) with a nonsignificant result ($p = 0.32$) for the older age group.

The role of age as a confounder differed for hypoxia and hypotension. If age was not controlled for in the analysis, the extremely strong independent association of hypotension with outcome remained unchanged. However, lack of control for age reduced the association of outcome with hypoxia for the extended time period although hypoxia continued to be an independent predictor of outcome.

Severe Multiple Trauma

Severe multiple trauma (AIS grade greater than 3) was more prevalent ($p = 0.017$) among patients less than 40 years old (22%) than among those more than 40 (13%) for the 717 patients studied. There was a significant trend for poorer outcome in patients with associated severe multiple trauma ($p = 0.0013$). When patients were stratified by age, the trend is pronounced, but not statistically significant, for those under age 40 years ($p = 0.22$) and minimal for those over 40 (Fig. 3). If hypoxia and hypotension were controlled for in the analysis in addition to age, however, severe multiple trauma was no longer statistically significant ($p = 0.22$). The conclusion is not that outcome over the long term was unaffected by severe multiple trauma, but rather that there was evidently no significant effect on outcome from severe

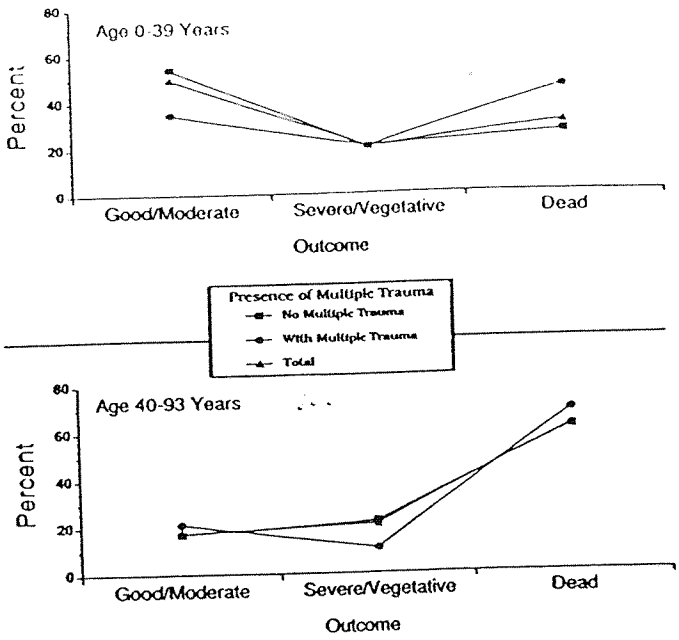

Figure 3. TCDB Data. Outcome by presence or absence of severe multiple trauma, stratified by age (n = 717).

multiple trauma once the effects of hypotension, hypoxia, and age were taken into account.

Tables giving a complete breakdown of the data by age, severe multiple trauma, hypoxia, hypotension, and outcome are available to interested readers upon request. They are not included here because of small cell sizes and their complexity. Tables 3 and 4 do not separate secondary insult categories by severe multiple trauma, but this factor was controlled for in the analysis.

We also evaluated the association between hypoxia, hypotension, and severe multiple trauma without regard to outcome. Log-linear modelling of three factor interactions for these categories was not significant ($p = 0.65$). Two-factor interactions, investigated using M-H analysis, revealed hypoxia to be significantly associated with hypotension controlling for severe multiple trauma ($p < 0.001$), and hypotension to be similarly associated with severe multiple trauma controlling for hypoxia ($p < 0.001$), whereas the association between hypoxia and severe multiple trauma controlling for hypotension did not reach significance ($p = 0.067$).

DISCUSSION

The present report clearly demonstrates the enormously adverse influence of hypotension on outcome from severe head injury. In 1978, Graham et al. reported finding ischemic neuropathologic conditions, excluding lesions felt to be a direct result of transtentorial herniation, in 91% of 151 nonselected and consecutive patients dying as a result of severe head injury.[10] Since a significant percentage was associated with evidence of increased intracranial pressure (ICP), that paper served as an impetus to our present recognition and treatment of elevated ICP in order to avoid compromised cerebral

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GLASGOW OUTCOME SCALE (GOS) DEFINITIONS

CATEGORIES OF SURVIVORS:

Good recovery

This need not imply the restoration of all normal functions; there may be persisting sequelae such as bilateral anosmia, or mild impairment on some psychological tests. But the patient is able to participate in normal social life and could return to work (although he/she may not have done so). Just as some moderately disabled patients do work, quite a number of those with good recovery do not - the possible reason for which are many.

Moderate disability (independent but disabled)

These patients look after themselves, can travel by public transport, and some are capable of work. This may be of a sheltered kind but certain disabilities are compatible with return to the patient's own occupation. For example, a patient with severe dysphasia may be able to carry out complex nonverbal tasks - one such man who was a shepherd could readily control his dogs by whistling. A patient with a blind eye would be in this category, or one who had bilateral deafness, because these are also compatible with economic independence in certain kinds of work.

Most patients in the category of moderately disabled have either memory deficits or personality changes, varying degress of hemiparesis, or dysphasia or ataxia, post-traumatic epilepsy, or major cranial nerve deficits.

Patients able to attend to their personal needs in their own room, but to do no more than this, would be judged severely disabled on the Glasgow Outcome Scale.

Severe disability

Patients in this category are dependent on some other person for some activities during every 24 hours. The worst affected are severely disabled physically, often with spastic paralysis of three of four limbs, sometimes with dyarthria and dysphasia as well. Marked physical deficits such as these are always associated with severely restricted mental activity; however, there are some patients who have little or no persisting neurological disability but who are so severely affected mentally, that they require permanent supervision, usually in a mental hospital. The least affected of those in the category of severe disability are patients who are communicative and sensible, though usually with marked impairment of cognitive and memory function on testing, who are dependent for only certain activities on others - perhaps dressing, feeding, or cooking their meals. Such a person could not be left to fend for himself, even for a weekend. He is not independent and must therefore be regarded as severely disabled on our classification.

Vegetative state

Patients do not show signs of any contact with their surroundings. May open their eyes (with sleep and wake rhythms), may be able to follow an object with eyes, but do not speak, do not obey commands and do not show a response that is psychologically meaningful to the objective observer.

perfusion pressure and resultant ischemia. In conjunction with the work of Miller et al.,[1-4] the TCDB data now explain another significant cause for the frequency of ischemic damage by elucidating the high incidence and grave consequences of early posttraumatic hypotension.

The occurrence of ischemic secondary insults to injured brains in this cohort was devastating and frequent (Table 2). The addition of hypotension with or without hypoxia doubles the mortality and significantly increases the morbidity of a severe head injury. The gravity of this relationship is magnified by the evidence that it occurred in 35% of a patient cohort that was admitted to centers with highly developed trauma treatment facilities.

The TCDB data also show hypoxia to have a significant influence on outcome from severe head injury, albeit to a lesser extent than hypotension. Although the presence of hypoxia alone only increased the overall mortality slightly, it was even more prevalent than hypotension, occurring in 46% of this TCDB patient cohort some time during the early posttraumatic period.

As demonstrated in Table 1, Miller et al. showed that patients who suffered hypoxia or hypotension as secondary insults did notably less well than those who did not. Tables 3 and 4, however, reveal that hypoxia exclusive of hypotension was far less influential in affecting outcome. This suggests that the subset of patients in the hypoxia group of Miller et al. who were also hypotensive was responsible in large part for the higher morbidity and mortality in their nonmutually exclusive hypoxia group. Since we do not have data to analyze the possibility that their hypoxic insults were more severe or protracted, which is possible given the subsequent improvements in field attention to airway management and oxygenation, we cannot exclude such an explanation. Given the magnitude of change in the impact of hypoxia on outcome when mutually exclusive groups were employed, however, it can be stated that hypotension was definitely the more damaging of the two insults.

Since secondary brain insults result from disturbances affecting the body in general, there is potentially a strong confounding of hypoxia and hypotension with the injuries that may be responsible for them. It is possible that the presence of severe multiple system injuries, and not hypoxia or hypotension per se, is the cause of the increased morbidity and mortality. In order to investigate this possibility, we studied the interaction of severe multiple injuries (AIS grade greater than 3) to one or more extracranial organ systems with hypoxia and hypotension to examine their relative influences on outcome from severe head injury. As is demonstrated by multivariable analysis of hypoxia, hypotension, age, and severe multiple injuries, the effects of secondary brain insults on outcome from severe head injury were independent of the presence or absence of associated severe multiple injuries. In particular, although there was a significant association between the occurrence of hypotension and the presence of severe multiple injuries, the adverse impact of hypotension with or without hypoxia persisted even when injuries of AIS grade > 3 were controlled for.

It has been well established that age is a strong determinant of outcome from a given head injury.[11-15] Recent analysis of data from the TCDB by Vollmer et al. revealed that age per se is a significant predictor of outcome, independent of confounding variables such as mechanism of injury, intracranial diagnosis, associated injuries, preinjury state of health, etc.[16] Using the same TCDB data, Marshall et al. reported that, when outcome by age is investigated in a year-by-year fashion, the age of 40 years appears to be the threshold beyond which outcome is clearly decremented based upon patient maturity alone.[17] In light of these reports, we have controlled for age, using 40 years as the dividing point. Our multivariable analysis, however, demonstrated that the addition of age into this analysis did not significantly affect the independent influence of secondary brain insults on outcome. This independence further underscores the important role that secondary insults can play in affecting prognosis after head injury.

Although it did not alter the statistical independence of hypoxia as an overall predictor of outcome, there was a significant interaction with age when data from the extended time period were examined. It is likely that this interaction would have had a stronger influence on the independence of hypoxia if the older age group had comprised a larger proportion of the sample. That the influence of hypoxia is somewhat confounded by age is likely related to its less dramatic overall impact on outcome, coupled with the very high baseline mortality in the older patient group for all categories. Its influence may also be tempered by the highly developed intubation and ventilation protocols employed by emergency medical services very early in field resuscitation. These would have the effect of both minimizing the impact of the episodes of hypoxia that were successfully treated in the field and of selecting out only the most resistant cases to be present by the time of arrival at the hospital. Finally, the diminished accuracy of using clinical signs of hypoxia in the absence of arterial blood gas values for this time period could be influential if hypoxia was overdiagnosed, although efforts were taken to include only reports of documented cyanosis or apnea.

The lack of a statistically significant association between hypoxia and severe multiple injuries when two-factor interactions were evaluated without respect to outcome suggests that a sizeable proportion of hypoxia may have been related to the head injury itself. Eighty-six percent of the patients suffering hypoxia did not have associated severe multiple injuries by our definition (unpublished TCDB data, 1991). Above and beyond the everpresent hazards of aspiration in comatose patients, the detrimental effects of head injury on pulmonary function are well known; shunting, neurogenic pulmonary edema, and frank apnea from an isolated cerebral injury could account for much of the hypoxia in these

cases.[18-21] Fortunately, in contrast to hypotension, we have made substantial progress in dealing with hypoxia during the early postinjury period.

The finding that the combination of hypoxia and hypotension at the time of arrival at the hospital negatively influenced outcome independent of the effects of hypoxia or hypotension alone illustrates the ominous impact of superimposing these two secondary brain insults. The grave prognostic significance of the coexistence of hypoxia and hypotension at the time of arrival at the hospital is reflected by the 75% mortality for patients with both insults (Table 3). The basis of the refractory nature of injury in this group of patients to treatment is unclear. Nevertheless, the implied benefits of shifting patients from this category into any other category underscores the value of an efficient and well trained prehospital response team.

The concept that hypotension negatively affects outcome from severe head injury is not new. Analyzing data from the pilot study for the TCDB, Eisenberg et al. showed that prehospital hypotension was predictive of significantly poorer outcome from severe head injury.[22] Using the same data base, Seelig et al. studied the first 72 hours after admission and found that hypotension was significantly associated with the development of sustained ICP elevations and uncontrollable ICP, with attendant high mortality.[23] Newfield et al. found that mortality was more strongly associated with hypotension than with GCS score or associated major extracranial injury in a series of 129 patients.[24] A recent report by Meguro and Tator, looking at hypotension associated with severe multiple injuries demonstrated poorer neurologic recovery and higher mortality from spinal cord or cauda equina injuries in patients with hypotension versus normotensive patients.[25]

The information we present here strongly corroborates the reports using the larger cohort of the TCDB. Furthermore, utilizing this cohort, we now can estimate the frequency of hypotension, the magnitude of its adverse influence, and its cardinal position in determining the outcome from severe head injury.

The disparity between hypotension and hypoxia as secondary brain insults lies in the differential sensitivity of the brain to oxygenation and perfusion. The highly developed ability of the brain to extract oxygen protects it from hypoxia if normal perfusion is maintained. In contrast, the disruption of autoregulation that occurs with head injury[1,26,27] results in ischemia from cerebral hypoperfusion resulting from systemic hypotension despite adequate oxygenation. During this loss of autoregulation, cerebral blood flow (CBF) is directly reflective of systemic arterial pressure, with poor maintenance of cerebral perfusion pressure and uncoupling of CBF from the cerebral metabolic rate for oxygen ($CMRO_2$) both globally and regionally.[1,26-29] Therefore, despite the benefits of aggressive prehospital pulmonary treatment, it can be powerfully neutralized if concomitant hypotension is not reversed.

The magnitude of the independent influence that hypotension has an outcome is remarkable. Given its frequency of occurrence and our relative inability to successfully treat it in the field, we see before us a clinical problem where any improvement has the potential of making a significant impact on the outcome from head injury. A key implication of the data presented here is the concept that sensitivity to hypotension of patients with head injuries makes them fundamentally different from other patients with multiple injuries. Episodes of hypotension that would be well tolerated by a patient with isolated abdominal trauma can apparently devastate a patient with an injured brain. This indicates the need for evaluating treatment modalities for hypotension using patients with head injury as the index. The roles of agents such as hypertonic saline, colloid versus crystalloid, pneumatic antishock garments, and inotropic or vasopressor drugs should be reviewed with respect to applicability in restoring or maintaining blood pressure during the early stages of resuscitation of brain injured patients. It may be appropriate to temporize with pressors in this patient group until adequate volume can be administered.

A proportion of secondary brain insults will not prove treatable or preventable. It is these insults that highlight the need to develop methods of preventing or diminishing their negative impact. The role of agents such as inhibitors of free radicals[30,31] or the excitotoxicity of acidic amino acids[32-35] as well as the possibility of employing agents such as nerve growth factor,[36,37] thyrotropin releasing factor,[38] opioid antagonists,[39,40] or G_{M1} ganglioside[41,42] need to be investigated in a search for possible pharmacologic antagonism of secondary brain insults. A multifaceted approach to brain trauma and secondary insults employing highly directed triage protocols and neuronal cytoprotective pharmacology is likely to be required if substantial improvement is to occur.

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ENDOTRACHEAL INTUBATION IN THE FIELD IMPROVES SURVIVAL IN PATIENTS WITH SEVERE HEAD INJURY

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Purpose: The importance of minimizing secondary insults to the injured brain is well established. Field airway control with assurance of adequate gas exchange is a key step. Many current field protocols allow endotracheal intubation only in patients with ineffective ventilation, without pharmacological assistance. We studied the effect of field intubation on mortality in patients with head injury (HI), in order to assess the possible benefit of extending indications for field intubation.
Methods: All patients with blunt mechanism of injury and field GCS ≤ 8 transported by ground ALS ambulance in a large urban county over a 4 year period were identified. Type of field airway, injury specific data, and final discharge disposition were evaluated. Two sub-groups were defined: Severe HI (Head/Neck AIS > 3) and Isolated HI (no other AIS component > 3). Mortality was compared between patients who were intubated in the field and those who were not. **Results:**

Group	N	Mortality	% Tubed
Severe HI	**671**		**58%**
Not Intubated	284	57%*	
Intubated	387	36%*	
Isolated Severe HI	**351**		**59%**
Not Intubated	145	50%*	
Intubated	206	23%*	
Isolated Severe HI, GCS = 3	**176**		**51%**
Not Intubated	86	69%*	
Intubated	90	41%*	
Isolated Severe HI, GCS > 3	**175**		**66%**
Not Intubated	59	22%*	
Intubated	116	9%*	

* denotes statistical significance at $p < 0.05$ by χ^2.

Conclusions: Field intubation is associated with a significant decrease in mortality in patients with severe HI, especially those with isolated injury. Only 50% - 60% of these patients were intubated under current protocol. Broadening the indications for field intubation has significant potential to improve the care of head injury patients.

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Selected Topics Prehospital Care

INTUBATION TECHNIQUES IN THE HELICOPTER

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☐ **Abstract—The purpose of this study is an analysis of 630 field intubations of trauma patients by flight personnel of the San Diego Life Flight program. We compared nasotracheal intubation to rapid sequence induction orotracheal intubation and noninduced orotracheal intubation. We measured success of intubation route, complications, and overall patient outcome. Flight records, quality assurance flight procedure data, and hospitalization data from the San Diego Trauma Registry were reviewed over a 4-year period, from 1988 to 1991. The results of our study show that rapid sequence induction orotracheal intubation has a higher success rate, fewer complications, and a better patient outcome compared to noninduced orotracheal intubation and blind nasotracheal intubation. We recommend that rapid sequence induction oral intubation be the standard method for prehospital airway management in trauma patients.**

☐ **Keywords—orotracheal intubation; nasotracheal intubation; helicopter; trauma**

INTRODUCTION

In 1870, during the Franco-Prussian War, the first medical "aeroevacuation" occurred when hot air balloons carried 160 injured Frenchmen to safety (1). The use of the helicopter as a successful aeromedical evacuation tool gained credibility in the Vietnam conflict, in which mortality from combat wounds decreased from 8.5% in World War I to less than 1% in Vietnam (2). Since then, civilian interest in the medical applications of helicopters has developed rapidly (3). The University of California, San Diego Medical Center has been a base for San Diego's Life Flight Emergency Helicopter Service since its beginning in 1980. Among the many advanced therapeutic modalities of the Life Flight program is the ability to offer active airway intervention and management to trauma patients. Our protocol mandates intubation for any patient with a Glascow Coma Score (GCS) ≤ 8 for controlling intracranial pressure, protecting against aspiration and ensuring adequate ventilation.

The four routes of intubation used are rapid sequence induction orotracheal (RSI), nonrapid sequence induction orotracheal (NRSI), blind nasotracheal (NT), and cricothyrotomy (CRIC). Of these, the RSI, NRSI, and NT methods are used routinely, while CRIC is used only in cases of failure of other airway adjuncts or in severe facial trauma. Extensive literature has described the efficacy, indications, and success rates of each of these routes in trauma patients (4–14); however, the choice of the optimal procedure, with a comparison of complications, success rates, and patient outcome, is not clear. The purpose of this study is to evaluate which route of intubation in trauma patients is superior with respect to success rates, complications, and overall patient outcome.

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MATERIALS AND METHODS

The San Diego Life Flight helicopter program is affiliated with one Level I and five Level II trauma centers located in San Diego County. These include the University of California, San Diego (UCSD) Medical Center (Level I), Mercy Hospital, San Diego Children's Hospital, Sharp Memorial Hospital, Scripps Hospital in La Jolla, and Palomar Medical Center (Level II). Crews on all flights during the study period included a flight nurse, paired with either another flight nurse, a paramedic, a second- or third-year emergency medicine resident, or an emergency medicine attending physician. Medical care on all flights during the study period were under the direction of the flight nurse, unless the crew was split for multiple injury scenes. All crew members other than paramedics are permitted to perform all routes of intubations; however, during the study period, no intubations were done by flight paramedics.

Crews are trained in airway management using cadaver, manikin, and animal models. Three times a year, crew members are required to attend surgical laboratories during which airway management skills are practiced. During initial training, new crew members are paired with senior flight crew members experienced in airway management. Individual airway management performance is monitored by the clinical specialist (RN), chief flight nurse, and medical director. If performance is felt to be substandard, the individual is required to obtain additional supervised training.

This study involves a review of flight data recorded during all Life Flight trauma responses over a 48-month period, between 1988 and 1991. To capture all patients in whom tracheal intubation attempts occurred, a list of flight numbers and dates of admission were generated from the Life Flight airway management quality assurance (QA) report, a form that must be filled out by crew members after any calls in which airway control is attempted. From this list, all nontrauma patients were eliminated (including interfacility transfers and medical emergencies), and any patients intubated prior to the arrival of Life Flight were also eliminated from the study in order to keep a consistent level of care throughout the study period. The patient data included patient sex, Champion Trauma Score (15), Crams Score (16), Glascow Coma Score at time of Life Flight arrival, and transport time. Information concerning airway management included airway type established, and the number of attempts by each crew member. An attempt was defined as a placement maneuver of the endotracheal tube, not just visualization of cords. Complications of intubation included esophageal intubation recognized by crew, esophageal intubation unrecognized by crew, mainstem intubation recognized by crew, mainstem bronchus intubation unrecognized by crew, tracheal stricture, tube too large, cuff torn or leaky, equipment problem (i.e., laryngoscope light did not function), laryngospasm, dysrhythmias, vomiting secondary to intubation attempts, inability to visualize cords, unintentional extubation in transit, epistaxis, broken teeth, and tracheal perforation. The parameters reviewed for cricothyrotomy were indications (failed oral or nasal intubation, airway obstruction, severe facial trauma, cervical spine injury, or other), and complications (severe hemorrhage, posterior tracheal perforation, esophageal placement, subcutaneous tissue placement, unable to pass tube, or other).

From the flight records, we obtained data on date of birth, scene time, and medications used during intubation attempts. We were unable to locate 10 flight records (5 NRSI oral intubations, 3 nasal intubations, and 1 no airway established from 1988; 1 cricothyrotomy from 1990), so these patients were excluded from analysis.

From the San Diego Trauma Registry, we obtained information regarding patient progress through hospitalization. The Trauma Registry consists of data for patients brought to one of the trauma centers meeting one of the following criteria: death, admission to the intensive care unit (ICU) or operating room (OR), or hospitalization of more than three days. Burn patients and drowning victims are not included in the Trauma Registry and were excluded from this study. In addition, three patients had to be excluded because they were still hospitalized at the conclusion of the study period and had incomplete records.

Information obtained from the Trauma Registry regarding potential complications of airway management during hospitalization include aspiration pneumonia, pneumothorax secondary to barotrauma, iatrogenic pneumothorax, dysrhythmias, cardiac arrest, sinusitis, anoxic encephalopathy, brain death, meningitis, progression of original neurological insult, and seizure. Patient outcomes were categorized as follows: death in the field, death in the hospital in fewer than 30 days, discharge to home or to jail, transfer to another hospital or to an extended care facility (ECF), or left against medical advice. We also reviewed the patient's total days spent in the hospital and total days in the ICU. The Trauma Registry supplied Probability of Survival score (PS) (17), Abbre-

viated Injury Scale (AIS) values, and Injury Severity Scores (ISS) (18) for each of the patients.

A successful intubation is defined as placement of the endotracheal tube in the trachea with the ability to ventilate the patient. Success is confirmed in every case by the operator via auscultation of lungs bilaterally, in addition to one or more of the following: direct visualization of tube through the cords, auscultation over stomach without breath sounds present, mist in the tube, and equal rise and fall of chest. Endotracheal tube placement was confirmed as correct by the trauma surgeon or anesthesiologist upon arrival at the trauma facility.

The patients in this study were divided into three groups: blind nasotracheal, NRSI, and RSI intubations. Prior to December 1989, the Life Flight teams used blind nasotracheal intubation as a means of airway management in about two-thirds of patients needing airway management, with NRSI orotracheal used for the majority of the rest. After November 1989, the protocol was changed to the use of RSI orotracheal intubation as the primary means of managing an airway in about three-fifths of patients, with a decrease in the frequency of utilization of the nasotracheal and NRSI orotracheal methods. The RSI patients were sedated with fentanyl (3 to 5 mcg/kg), premedicated with lidocaine (1 mg/kg), and paralyzed with succinylcholine (1 to 1.5 mg/kg), along with a simultaneous Sellick maneuver to prevent regurgitation (19). Further sedatives and paralytics were given postintubation as needed. Nasally intubated patients were treated with neosynephrine intranasally, then had a nasal trumpet lubricated with xylocaine jelly passed as a dilatator. The endotracheal tube was then passed after the trumpet was removed.

We studied the three patient groups with respect to the number of attempts and successes in the 24-month interval before and after December 31, 1989. We also compared immediate and delayed complication rates, and patient outcome among the three groups. When comparing incidence of complications, patients dead on scene were incorporated into the totals of "complications noted in the field or trauma resuscitation," but were eliminated from the totals of "complications noted during the hospitalization," because patients dead on scene did not meet Trauma Registry criteria, and, thus, data were not available. Permission for the study was obtained from the UCSD human rights study committee.

Statistical significance was tested using analysis of variance for continuous variables and using bivariate categorical analysis and Chi-square tests for categorical variables (sex, complication rates). Significance was assigned a value of $P < 0.05$. All tests were two-sided.

RESULTS

During the 4-year study period, 630 trauma patients were intubated or had intubation attempted by the Life Flight crews and were admitted to one of the six trauma centers. Of these patients, 580 met criteria for inclusion in the study in that they died, were admitted to the SICU or OR, or were hospitalized for more than 3 days, with the other 50 patients having fallen outside these criteria or admitted as drowning or burn patients. Drowning and burn patients were considered specialized admissions and were not included in this study. A total of 567 complete records were found and used in the study.

Of the 538 patients who had an airway established during the study period, 237 (44%) were nasally intubated, 143 (27%) were NRSI orally intubated, 140 (26%) were RSI orally intubated, and 18 (3%) were surgically obtained via cricothyrotomy. Twenty-nine patients did not have an airway established despite attempts. Demographic data comparing the three groups is included in Table 1. Data comparing successes of the three groups distributed by years are shown in Table 2.

Table 3 shows the total attempts, total number of patients in whom intubation was attempted, and the total number of successful intubations for each technique. The data showed 75% of patients with nasal attempts were successfully intubated nasally. This compares with 84% for NRSI attempts and 90% for RSI oral attempts. These data include patients in whom more than one technique may have been used.

The success rate for each intubation technique, when that method was used as an initial attempt, is displayed in Table 4. Of the patients in whom nasotracheal intubation was initially attempted, 74% were successfully nasally intubated. RSI orotracheal intubation was initially successful in 88% of patients, and NRSI orotracheal intubation was successful in 90% (Table 4).

Of the 133 patients in whom RSI orotracheal was initially attempted, 11 (8%) failed to be intubated but were successfully intubated nasally, while 23 (10%) of 222 patients in whom nasal intubation was initially attempted failed to be intubated and were subsequently successfully intubated via the RSI orotracheal route, and another 23 (10%) went on to successful NRSI orotracheal intubation. Of the 134 patients in whom intubation was initially attempted via

Table 1. Demographic Data Comparing the Methods

Statistic	Mean				
	Nasal (n = 237)	NRSI Oral (n = 143)	RSI Oral (n = 140)	*P*-value[1]	*P*-value[2]
Age	30	31	26	†	†
Sex (% male)	83	76	76		
ISS	30.5	23.0	24.7	‡	‡
AIS score:					
Head/neck	4.1	4.4	3.9	‡	‡
Face	2.2	2.2	2.1		
Chest	3.4	3.9	3.2		
Abdomen	3.0	3.7	3.0	*	†
Extremity or pelvic	2.6	2.6	2.6	†	
External	1.3	1.3	1.3	‡	
PS Value	.66	.37	.75	‡	*
Crams Score	4.9	2.1	5.4	‡	†
Champion Trauma Score	10.4	4.4	11.0	‡	*
GCS initially	5.9	4.0	6.5	‡	*
Scene time (min)	21	23	25	‡	‡
Transport time (min)	10	10	11	†	

NRSI = nonrapid sequence induction; RSI = rapid sequence induction; ISS = injury severity score; AIS = abbreviated injury scale; PS = probability of survival; GCS = Glascow coma scale.
[1]Comparison across all three groups.
[2]Comparison between nasal and RSI oral.
*P value < 0.05.
†P value < 0.01.
‡P value < 0.001.

the NRSI method, 4 (3%) went on to successful nasal intubation, and no RSI oral attempts were made in this group.

Percentages in Table 5 and 6 represent incidence of complications, although some of the patients may have had more than one complication. One hundred ninety-three total complications were noted in the field or resuscitation for the three groups. Fifty-five were in nasotracheally intubated patients (n = 237), 12 were in RSI orotracheally intubated patients (n = 140), and 126 were in patients intubated via the NRSI orotracheal method (n = 143). This corresponds with 23% of nasal, 88% of NRSI oral, and 9% of RSI oral patients having complications (Table 5). Analysis of delayed complications revealed nine nasotracheal intubation complications in 237 patients, and one each for NRSI orotracheal and RSI orotracheal in 87 and 137 patients, respectively (Table 6).

Data concerned with patient outcome are shown in Table 7.

Table 2. Distribution of Attempted Intubations by Years

Statistic	N (%)	
	1988–1989 (n = 289)	1990–1991 (n = 278)
Successful intubations	263 (91)	275 (99)
Successful nasal intubations	167 (58)	70 (26)
Successful NRSI oral intubations	90 (31)	53 (19)
Successful RSI oral intubations	0 (0)	140 (51)
Successful cricothyrotomies	6 (2)	12 (4)
No airway established	26 (9)	3 (1)

NRSI = Nonrapid sequence induction; RSI = rapid sequence induction.

DISCUSSION

Success Rates

Our study shows that only 75% of 315 patients were successfully intubated nasally. This compares to 84% of 170 patients intubated via NRSI orotracheal intubation, and 90% of 156 patients intubated with the RSI oral method.

Table 3. Success Rate for Each Technique Overall

Airway Type	N			
	Total Attempts	Total Patients Attempted	Total Successes	% Successful
Nasal	455	315	237	75
NRSI	220	170	143	84
RSI	226	156	140	90

NRSI = nonrapid sequence induction; RSI = rapid sequence induction. More than one technique may have been used for a single patient.

Table 4. Success Rate for Each Technique as an Initial Attempt

Airway Type	N		
	Patients Attempted	Total Successful	% Successful
Nasal	300	222	74
RSI	133	117	88
NRSI	134	120	90

NRSI = nonrapid sequence induction; RSI = rapid sequence induction.

Our 75% success rate of nasal intubation in 315 patients is much lower than Tintinalli and Claffey's (10) 91% success in 71 patients, Danzl and Thomas's (11) 92% success in 300 patients, or Iserson's (12) 92% success in 138 patients. However, it should be noted that these procedures were done in a semicontrolled hospital emergency department (ED) setting, versus our procedures that were done at the scene under various weather, lighting, and environmental conditions. Some patients were even intubated prior to extrication.

With regard to NRSI orotracheal intubation, our study shows an 84% success in 170 patients. This can be compared to the studies of Stewart and colleagues (20), who showed 90% success of 779 patients intubated by paramedics with NRSI orotracheal intubation; DeLeo (21), in which 90.6% of 785 patients were successfully intubated by rescue squad personnel; and Pointer (22), in which paramedics intubated 93.5% of 383 patients using this method. Our success rate may be lower because our crews have the capability to go on to other methods of airway management (RSI oral or cricothyrotomy). So, after two or three NRSI oral failures, the Life Flight crews usually choose another method, whereas, in the previous studies, paramedic crews were making up to six attempts before attaining success. Moreover, all of our subjects were trauma patients; no medical arrests were included.

Ours study shows 90% of 156 patients successfully intubated via the RSI orotracheal method. This is comparable to the results of Thompson and colleagues (23), who had 42 of 46 (91%) successes in the emergency department with RSI orotracheal intuba-

Table 5. Complications Noted in the Field or Trauma Resuscitation: Comparison of Methods

Complication	N (%)				
	Nasal (n = 237)	NRSI Oral (n = 143)	RSI Oral (n = 140)	*P*-value[1]	*P*-value[2]
Esophageal intubation-unrecognized	0 (0)	0 (0)	0 (0)		
Esophageal intubation-recognized	8 (3)	28 (20)	5 (4)	‡	
Mainstem intubation-recognized	5 (2)	2 (1)	1 (1)		
Mainstem intubation-unrecognized	7 (3)	11 (8)	0 (0)	‡	*
Stricture encountered	1 (0.5)	2 (1)	0 (0)		
Tube used was too large	7 (3)	7 (5)	2 (1)		
Cuff torn or leaky	2 (1)	7 (5)	0 (0)	†	
Equipment problem	3 (1)	7 (5)	0 (0)	†	
Laryngospasm	4 (2)	7 (5)	0 (0)	*	
Dysrhythmias	0 (0)	5 (4)	1 (1)	†	
Vomiting	2 (1)	21 (15)	0 (0)	‡	
Unable to visualize	0 (0)	24 (17)	3 (2)	‡	
Extubated in transit	2 (1)	1 (1)	0 (0)		
Epistaxis	3 (1)	2 (1)	0 (0)		
Broken teeth	0 (0)	2 (1)	0 (0)		
Tracheal perforation	1 (0.5)	0 (0)	0 (0)		
Total	55	126	12	‡	*

NRSI = nonrapid sequence induction; RSI = rapid sequence induction.
[1]Comparison across all three groups.
[2]Comparison between nasal and RSI oral.
*P value < 0.05.
†P value < 0.01.
‡P value < 0.001.

Table 6. Complications Noted During Hospitalization: Comparison of Methods

Complication[1]	N (%) Nasal (n = 237)	NRSI Oral (n = 87)	RSI Oral (n = 137)
Pneumothorax (barotrauma)	1 (0.5)	0 (0)	0 (0)
Pneumothorax (latrogenic)	0 (0)	1 (1)	0 (0)
Dysrhythmias	2 (1)	0 (0)	0 (0)
Cardiac Arrest (unexpected)	2 (1)	0 (0)	0 (0)
Disseminated intravascular coagulation	0 (0)	0 (0)	0 (0)
Sinusitis	1 (0.5)	0 (0)	1 (1)
Anoxic encephalopathy	0 (0)	0 (0)	0 (0)
Brain death	0 (0)	0 (0)	0 (0)
Meningitis	2 (1)	0 (0)	0 (0)
Progression of original neuro insult	1 (0.5)	0 (0)	0 (0)
Seizure	0 (0)	0 (0)	0 (0)
Aspiration pneumonia	0 (0)	0 (0)	0 (0)
Total	9	1	1[2,3]

NRSI = nonrapid sequence induction; RSI = rapid sequence induction.
[1]No individual complication had a P value < 0.05.
[2]Comparison across all three groups gave P value of .051.
[3]Comparison between nasal and RSI oral gave P value of .057.

tion. Syverud and colleagues (6) had 95% success in 39 helicopter transported trauma patients who underwent RSI orotracheal intubation at the scene after failure of another method.

Success : attempts ratios for the three methods are as follows: nasotracheal, 237/455 = .52; NRSI orotracheal, 143/220 = .65; and RSI orotracheal, 140/226 = .62. The NRSI orotracheal ratio probably was higher than the other two methods because if this method failed, an alternate method would be used earlier, rather than continuing repeated attempts. Comparable studies for comparison were not available for nasal and RSI oral intubations. Stewart and colleagues (20) had a slightly higher success : attempts ratio of .57 (701/1240) for NRSI orotracheal intubations by paramedics. Pointer's (22) paramedic study had an NRSI oral success : attempts ratio of .69 (358/517), very comparable to our .65 value. It should be noted that these studies also included nontrauma patients.

Complications

Our study showed a 1% incidence of epistaxis in 237 nasally intubated patients. Tintinalli and Claffey (10) described 13 (18%) episodes of epistaxis in 71 ED nasally intubated patients. Danzl and Thomas (11) recorded 5 (2%) of 276 nasally intubated patients with severe epistaxis. Iserson (12) reported minimal epistaxis in about 40% of the 300 patients studied, and O'Brien and colleagues (4) reported a 3% incidence of epistaxis in 65 nasally intubated patients. These varying reports probably arise secondarily to one's definition of epistaxis. Our definition is profuse bleeding continuing after the tube is secured.

Table 7. Patient Outcome: Comparison of Techniques

Statistic	N (%) Nasal (n = 237)	NRSI Oral (n = 143)	RSI Oral (n = 140)	P-value[1]	P-value[2]
Discharge to home	84 (35)	17 (12)	68 (49)	‡	*
Transfer to extended care facility	57 (24)	13 (9)	21 (15)	†	
Transfer to another hospital	24 (10)	3 (2)	11 (8)	†	*
Average days hospitalized	21.8	17.1	14.4		
Average days in the ICU	8.1	5.9	6.6		

NRSI = nonrapid sequence induction; RSI = rapid sequence induction; ICU = intensive care unit.
[1]Comparison across all three groups.
[2]Comparison between nasal and RSI oral.
*P value < 0.05.
†P value < 0.01.
‡P value < 0.001.

We found 1% (1 of 140) of patients intubated with the RSI orotracheal method developed cardiac dysrhythmias, which included premature ventricular complexes, ventricular tachycardia, ventricular fibrillation, supraventricular tachycardia, or asystole. Syverud and colleagues (6) described a 23% (16 of 71) occurrence of dysrhythmias in RSI orally intubated patients. Roberts and colleagues (24) reported 21% (22 of 107) of patients developing dysrhythmic complications. Dysrhythmias may have been more common in these other two studies than in our study because we premedicate all RSI patients with lidocaine, whereas, Syverud and colleagues' study (6) shows a protocol of lidocaine as "recommended to prevent rise of intracranial pressure associated with intubation," and Roberts and colleagues (24) did not even list lidocaine premedication as part of protocol.

Our study showed a 0% occurrence of unrecognized esophageal intubations in 143 NRSI orally intubated patients compared with Pointer (22), who noted a 1% (5 of 383) incidence of unrecognized esophageal intubations, and Stewart and colleagues (20), who described a 0.5% (3 of 701) occurrence of unrecognized esophageal intubations.

Regarding the delayed complications, the actual complication cannot always be shown to be caused directly by the intubation; however, the intubation may have added increased risk for having the complication. Nasotracheal complications of interest included two cases of meningitis, with no cases reported in either of the oral groups. No cases of aspiration pneumonia were noted in any of the groups. This may be due in part to the low incidence of vomiting in the nasal and RSI oral groups along with the use of cricoid pressure during RSI oral intubation.

Patient Outcome

Patient outcome was evaluated by reviewing patient disposition and hospital days (see Table 7). No similar studies were found for comparison. Regarding disposition, 49% of RSI orally intubated patients were discharged to home, while only 35% of nasally intubated patients and 12% of NRSI orally intubated patients were discharged to home. Nine percent of NRSI oral patients were discharged to extended care facilities, compared with 15% of RSI oral patients and 24% of nasal patients. A NRSI orotracheal intubation was used mainly in apneic, more critically injured patients. Thus, more of these patients died, either in the field or in hospital, and fewer were discharged either to home or to an extended care facility.

The RSI orally intubated patients spent an average of 14.4 total days in the hospital. The NRSI oral patients spent an average of 17.1 days in the hospital, and nasally intubated patients spent an average of 21.8 days in the hospital. The NRSI orally intubated patients probably had a fewer number of days in the hospital because many of these patients were more critical and died during hospitalization, thus shortening their stay. This also holds true for the ICU data. Although the majority of nasal intubations occurred in 1988–1989, and all of the RSI oral intubations were in 1990–1991, a national trend toward shorter hospitalizations does not fully explain why, in two groups of patients with comparable injuries, the average RSI oral patient was discharged more than 7 days earlier than nasally intubated patients.

CONCLUSIONS

No individual method for intubating a trauma patient at the scene has gained a reputation of superiority over the others. Until now, the three main methods of field airway management, nasotracheal, RSI orotracheal, and NRSI orotracheal, had not been compared to one another in a single study.

Our study shows that RSI oral intubation has a higher success rate than the other two methods. Success : attempts ratios show that RSI orotracheal intubation takes no more attempts than successful NRSI oral intubation and fewer attempts than nasal intubation. The RSI oral intubations have significantly fewer immediate complications compared to the other two methods, and fewer delayed complications than nasal intubations. The RSI and NRSI oral intubations have the same number of delayed complications. Patients intubated via the RSI oral method are discharged to home more frequently and to extended-care facilities less frequently than nasally intubated patients. Total time spent in the hospital is significantly less for RSI intubated patients compared to the other two methods.

The results of our study show that rapid sequence induction orotracheal intubation has a higher success rate, fewer complications, and produces better patient outcome compared to noninduced orotracheal intubation and blind nasotracheal intubation. Thus, we recommend that RSI oral intubation be the method of choice for trauma airway management in the helicopter.

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Clinical Considerations in the Reduction of Secondary Brain Injury

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Craniocerebral trauma renders the brain vulnerable to a variety of secondary insults that must be prevented or promptly corrected before irreversible neurologic damage occurs. These secondary insults can include hypoxia, ischemia, or both, which result in significant cell loss. The trauma-induced state of vulnerability appears to be due to cellular ionic and metabolic alterations that make up the basic physiologic sequelae after brain injury. We discuss clinical aspects regarding these potentially devastating injuries in an effort to enhance their recognition and aid in their management.

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INTRODUCTION

Trauma can affect all segments of our population, and in the majority of trauma patients, head injury is the leading cause of morbidity and mortality. The impact on our health care system is immense as more than 500,000 people suffer head trauma annually in the United States.[1,2] In the past, patients with traumatic brain injuries were viewed with a certain degree of pessimism because both surgical and medical treatments were limited. However, advances in the past two decades have shown that prompt and intensive management leads to a significant improvement in outcome.[3,4] One of the major reasons for the increased number of patients making a good recovery has been the recognition and prevention of disorders that can cause secondary brain injury.

Recovery after traumatic brain injury is related to both the severity of the initial mechanical trauma and the presence of secondary insults. By definition, primary traumatic injury occurs immediately on impact. This may lead to irreversible damage that results from direct mechanical cell disruption and is dependent on the cause and severity of the inciting injury. Secondary injuries (or insults) are physiologic events occurring within minutes, hours, or

days after the primary injury and may lead to further damage of nervous tissue, prolonging and/or contributing to neurologic deficits.

The fact that secondary insults are adversely associated with outcome is epitomized by the so-called "talk-and-deteriorate" patients who are able to talk after their initial injury but ultimately die. These patients clearly demonstrate that the primary mechanical injury is not the sole determinant of outcome. Rose et al found that nearly one third (116) of their head-injured patients who died were in the "talk and deteriorate" category and identified the presence of an avoidable secondary insult in almost 75% of this group.[5] To further emphasize the impact of secondary injuries, two of the most common insults—hypotension and hypoxia—have been associated with a doubling of mortality after head trauma.[6] Although little can be done to alter the detrimental effects of the primary mechanical injury, timely and meticulous management avoids secondary injury and leads to a better neurologic recovery.

CAUSES OF SECONDARY BRAIN INJURY

Initial management of the patient with a severe head injury has two primary goals. The first is the immediate diagnosis of potentially treatable surgical lesions such as subdural, epidural, or intraparenchymal hematomas. The second objective during the emergency resuscitation of the head-injured patient is the recognition and prevention of conditions known to cause secondary brain injury. These conditions can be divided conveniently into systemic and intracranial disorders (Figures 1 and 2). Ideally, the management concepts of minimizing secondary brain injury should be initiated at the scene of the accident. These include adequate ventilator support for the patient with respiratory compromise and maintenance of adequate systemic blood pressure. The majority of systemic insults can be readily prevented or diagnosed and treated in the emergency department.

Figure 1.
Systemic secondary insults and their potential causes

Hypoxia	Respiratory arrest
	Airway obstruction
	Adult respiratory arrest syndrome
	Aspiration pneumonia
	Pneumothorax/hemothorax
	Pulmonary contusion
Hypotension	Shock
	Excessive bleeding
	Myocardial infarction
	Cardiac contusion or tamponade
	Spinal cord injury
	Tension pneumothorax
Electrolyte Imbalance	Diabetes insipidus
	Syndrome of inappropriate secretion of antidiuretic hormone
Others	Anemia
	Hyperthermia
	Hypercarbia
	Hypoglycemia

Systemic Insults Of the various systemic insults, hypoxia and hypotension are the most significant. Arterial hypoxemia commonly is observed on admission to the hospital and usually is due to a prolonged apneic period in the field. At the moment of impact, brain deformation and movement occur. Brain stem movement has been thought to be responsible for the loss of consciousness that commonly occurs after significant head trauma.[7] Because this vital structure also controls respiration, hypoventilation with prolonged apnea resulting in hypoxemia, hypercarbia, or atelectasis may occur. Thus, comatose head-injured patients should be treated rapidly with positive-pressure ventilation. Other causes of hypoxia, especially in the patient with multiple associated injuries, should be sought, including upper airway obstruction, pneumothorax, and pulmonary edema (Figure 1).

The presence of hypoxemia, regardless of the cause, has been associated with increased mortality. In 1977, Miller and Becker reported that mortality increases from 24% to 50% when hypoxemia occurs in association with head trauma.[6] However, a recent report from the Traumatic Coma Data Bank did not find hypoxia (PaO_2 less than 60 mm Hg) to be associated with increased mortality.[8] This is most likely due to increased awareness during the past decade of the detrimental effects caused by this secondary insult, resulting in a more rapid reversal of hypoxemia in the acute setting.

Hypotension (systolic blood pressure less than 90 mm Hg) accompanies head trauma in 35% of severely injured patients and increases mortality from 27% to 50%.[8] Hypotension reduces cerebral perfusion pressure (mean arterial pressure minus intracranial pressure), thus

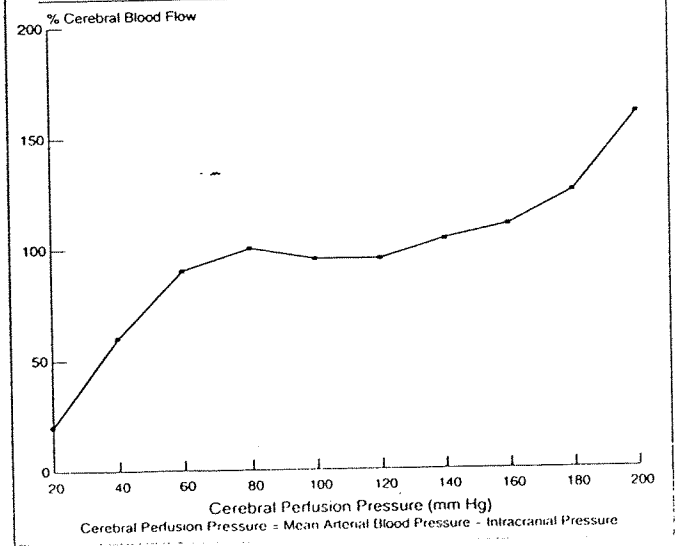
Figure 2.
Intracranial secondary insults

- Intracranial hypertension
- Delayed intracerebral hematoma
- Brain edema
- Hyperemia
- Carotid artery dissection
- Seizures
- Vasospasm

promoting cerebral ischemia and infarction. This is particularly harmful in the face of elevated intracranial pressure. Compounding the effect of hypotension is the fact that both impaired cerebral autoregulation and an uncoupling of blood flow and metabolism often are present after brain injury.[9,10] With normal autoregulation, cerebral blood flow remains constant despite fluctuation in mean arterial pressure between 60 and 180 mm Hg (Figure 3).This exquisitely sensitive mechanism causes arteriolar constriction or dilatation in response to either a rise or fall in mean arterial pressure, respectively. However, when this normal response is impaired, cerebral blood flow is related directly to systemic arterial pressure.Thus, if hypotension exists, reduced cerebral perfusion may result in tissue ischemia.This phenomenon explains the occasional patient whose neurologic examination improves dramatically after resuscitation and restoration of normal arterial blood pressure.

Anemia (hematocrit of less than 30) leads to reduced blood oxygen-carrying capacity and can potentiate cerebral ischemia. It usually is present in patients who have multiple injuries such as abdominal or thoracic trauma and often is seen in conjunction with arterial hypotension. Miller and Becker found a mortality rate of 52% when anemia accompanied head injury.[6]

Figure 3.
Normal cerebral autoregulation curve. Cerebral blood flow remains fairly constant despite fluctuations in mean arterial pressure between 60 and 180 mm Hg. However, when mean arterial pressure is markedly reduced or elevated, or autoregulation is impaired, cerebral blood flow is related directly to mean arterial pressure.

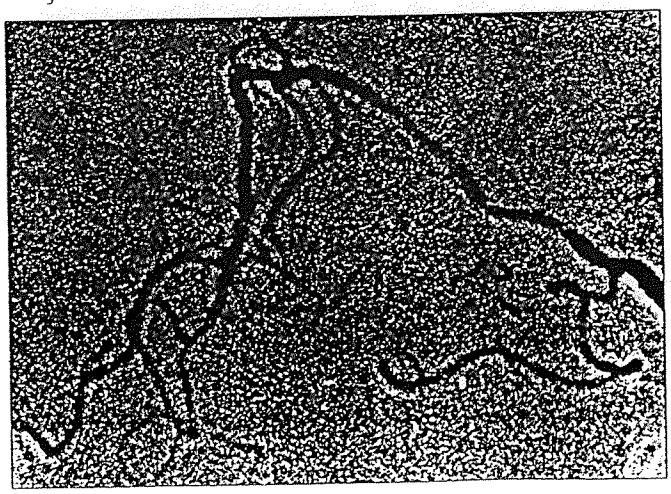


Other systemic causes of secondary injury that are not as common as those already described include electrolyte disturbances, hypoglycemia, and hyperthermia. Their association with head injury and bearing on outcome have not been definitively elucidated.

Intracranial Insults Acute traumatic mass lesions can directly compress vital brain areas or produce intracranial hypertension resulting in damage to viable tissue. It is clear that a delay in treatment adversely affects outcome. In patients with acute subdural hematomas, Seelig et al found a 90% mortality rate in patients who had their operation after four hours compared with a mortality rate of only 30% in those who had surgery within four hours.[11] Without the removal of large traumatic mass lesions (eg, intra-axial or extra-axial hematomas), intracranial pressure can rise progressively secondary to clot propagation or edema formation.

Intracranial hypertension can be caused by traumatic hematomas, cerebral edema, or cerebral hyperemia. Prolonged elevations of intracranial pressure are associated with a poor outcome, and a report from the Traumatic Coma Data Bank of 428 patients with severe head injury demonstrated a strong association between the duration of intracranial hypertension (intracranial pressure of more than 20 mm Hg) and outcome.[12,13] Raised intracranial pressure may cause secondary injury by promoting ischemia or causing direct compression of vital brain structures through the well known phenomenon of cerebral herniation. Brain herniation can further potentiate ischemia by compressing cerebral arteries. Current neuro-

Figure 4.
Lateral vertebrobasilar angiogram demonstrating diffuse post-traumatic basilar artery vasospasm. This occurred several days after a severe closed-head injury in a young man.



surgical management focuses on the aggressive management of elevated intracranial pressure, through both medical and surgical means, and has been shown to improve outcome significantly.[12,14]

Cerebral vasospasm is a common delayed complication of aneurysmal subarachnoid hemorrhage and is associated with the presence of subarachnoid blood.[15] Before the advent of computed tomography, angiography was a primary diagnostic modality in head-injured patients and occasionally demonstrated arterial spasm. However, with the routine use of computed tomography, angiography has been abandoned, and arterial spasm has been virtually forgotten as a complication of craniocerebral trauma. transcranial Doppler ultrasonography is a new technique that reliably assesses blood flow velocity in the basal cerebral arteries and is well suited for the detection of vasospasm. We recently used transcranial Doppler ultrasonography to monitor serially 30 closed-head injury patients (Figure 4) and found the incidence of post-traumatic spasm to be 30%.[16] Furthermore, the presence of arterial narrowing was associated with subarachnoid blood, decreased cerebral blood flow (one patient exhibited extensive cerebral infarction), and a worse neurologic outcome. The occurrence of vasospasm after craniocerebral trauma is not surprising because head injuries are the most common cause of subarachnoid hemorrhage. Increased recognition of vasospasm as a complication of head injury may result in appreciation of it as a significant secondary insult.

CELLULAR AND EXTRACELLULAR DERANGEMENTS AFTER TRAUMATIC BRAIN INJURY

After traumatic brain injury, some cells are damaged directly and irreversibly. However, other cells may be compromised functionally but are not disrupted mechanically and will recover if provided an optimal environment for survival. These compromised cells are particularly vulnerable to the pathophysiologic challenges imposed by secondary insults. Becker et al proposed the concept of protecting cells made vulnerable by cerebral injury,[17] and recent investigations have focused on this concept.

After the primary mechanical brain injury, alterations in the intracellular and extracellular environment occur that may be deleterious to cells. Important ionic concentration disturbances have been demonstrated, of which potassium and calcium have been the best studied.[18,18,19] These injury-induced ionic fluxes appear to be caused by massive release of excitatory amino acids (eg, glutamate), which have been shown to occur immediately after traumatic brain injury.[18] Ionic destabilization requires cells to use much of their energy resources to support ionic pumping mechanisms to restore a normal ionic environment. This may interfere with the energy requirements for normal cellular function such as protein synthesis. It recently has been shown that these increased energy demands are satisfied by hyperglycolysis; because oxidative metabolism is not relatively affected to the same degree as glucose metabolism, accumulation of lactate occurs.[20] This culminates in cellular acidosis, which may potentiate further injury and interfere with the restoration of ionic homeostasis.

Free radicals, including powerful oxidizer species, can readily oxidize other biologic molecules and have been hypothesized to play a role in the physiologic events leading to secondary injury.[21] Tissue injury leads to the formation of free radicals. If naturally occurring antioxidative pathways become saturated, cell membrane oxidation occurs by a process known as lipid peroxidation, and membrane disruption results. This produces further generation of lipid radical species, and a self-perpetuating cycle causing cellular damage is created. Lipid peroxidation occurs by a chain reaction that continues until a chain-breaking event occurs.[22] With the loss of membrane integrity, ionic fluxes occur, leading to increased energy demands to maintain homeostasis.

The cerebral areas affected by trauma-induced ionic and metabolic disturbances are particularly susceptible to a second insult and must be protected from these potentially lethal injuries immediately after the primary mechanical injury. With time, the injury-induced extracellular and intracellular alterations are corrected, and normal cellular function resumes, resulting in dissipation of enhanced cellular vulnerability.

New pharmacologic therapies aimed at restoring a more normal extracellular milieu are being investigated. Tris (hydroxymethyl) aminothane (THAM), a systemic and intracellular alkalinizing agent that crosses the blood-brain barrier, has been shown to reduce cerebral spinal fluid lactate levels after traumatic brain injury.[23] This suggests that THAM acts as a buffering agent to raise cellular pH, thereby countering adverse effects of excessive lactate production and acidosis. In some studies, THAM has been shown to improve survival, but other studies have not been so encouraging.[23,24] Several new drugs classified as free radical scavengers, designed to inhibit the destruction caused by lipid peroxidation, are under investigation. U-74006F, a 21-aminosteroid lacking glucocorticoid activity, has shown the most promise in animal studies.

and a multicenter clinical trial using this agent after head injury is in progress.

Although progress has been encouraging, further insight into the basic mechanisms that predispose cells to secondary injury is needed. A better understanding of the toxic environment to which cells are exposed after traumatic brain injury will allow the development of new therapeutic regimens that can provide the appropriate milieu for cell recovery and sustained viability. These new treatments need to not only improve cell survival but also increase their ability to respond in a way conducive to functional recovery, ultimately leading to improved patient outcome.

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